Effects of Sedentary Behaviour Interventions on Biomarkers of Cardiometabolic Risk in Adults: Systematic Review with Meta-analyses

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Highlights

- We evaluated the evidence regarding the impact that interventions to reduce sedentary behaviour (sitting), alone or in combination with physical activity increases, may have on important indicators of cardiometabolic risk, when intervening for ≥ 7 days under free-living conditions.
- Available evidence for different outcomes ranged from 6 to 25 controlled trials. On average, these interventions led to modest improvements in selected indicators of body anthropometry, glucose and lipid metabolism, and blood pressure regulation, with no adverse effects observed.
- Our review noted potential improvements for future research: more high-quality studies and interventions > 12 months; more population diversity (based on ethnicity, age, and clinical factors); more sensitive biological indicators; and, more studies evaluating vascular function and inflammation.

Running heading: Sedentary Behaviour Interventions and Cardiometabolic Risk

ABSTRACT

Context/Purpose: Observational and acute laboratory intervention research has shown excessive sedentary time is associated adversely with cardiometabolic biomarkers. This systematic review with meta-analyses synthesises results from free living interventions targeting reductions in sedentary behaviour alone or combined with increases in physical activity.

Methods: Six electronic databases were searched up to August 2019 for sedentary behaviour interventions in adults lasting for ≥ 7 days publishing cardiometabolic biomarker outcomes covering body anthropometry, blood pressure, glucose and lipid metabolism, and inflammation (54 studies). The pooled effectiveness of intervention net of control on 15 biomarker outcomes was evaluated using random effects meta-analyses in the studies with control groups not providing other relevant interventions (33 studies; 6 to 25 interventions analysed).

Results: Interventions between 2 weeks and < 6 months in non-clinical populations from North America, Europe and Australia comprised much of the evidence base. Pooled effects revealed small, significant ($p < 0.05$) beneficial effects on weight (≈ -0.6 kg), waist circumference (≈ -0.7 cm), percentage body fat (≈ -0.3 %), systolic blood pressure (≈ -1.1 mmHg), insulin (≈ -1.4 pM) and HDL cholesterol (≈ 0.04 mM). Pooled effects on the other biomarkers ($p > 0.05$) were also small, and beneficial in direction except for fat-free mass (≈ 0.0 kg). Heterogeneity ranged widely ($I^2 = 0.0$ to 72.9).

Conclusions: Our review of interventions targeting sedentary behaviour reductions alone, or combined with increases in physical activity, found evidence of effectiveness for improving some cardiometabolic risk biomarkers to a small degree. There was insufficient evidence to evaluate inflammation or vascular function. Key limitations to the underlying evidence base include a paucity of high-quality studies, interventions lasting for ≥ 12 months, sensitive biomarkers and clinical study populations (e.g., type 2 diabetes).

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Key words: Intervention, sedentary behaviour, sitting, physical activity, lifestyle, systematic review, meta-analysis, cardiovascular disease, adiposity, cardiometabolic

1. INTRODUCTION

Globally, cardiovascular diseases are the leading cause of death and a major cause of disability and lost productivity in adults [1, 2]. Estimates from 2017 also indicate that 451 million people are living with diabetes: a figure projected to rise to 693 million (≈10% of the population) by 2045 [3].

The evidence tends to indicate that greater time spent in sedentary behaviour (i.e., sitting / reclining at <1.5 Metabolic Equivalents [MET]) [4] is adversely associated with the risk of cardiovascular disease, type 2 diabetes and some cancers [5, 6] and with levels of a range of cardiometabolic risk biomarkers [7, 8]. A less prolonged sedentary accumulation pattern (i.e., more regular breaks, shorter sedentary bouts) has also been associated with lower body mass index [8]. It has largely been acute laboratory interventions (<7 days) using structured protocols providing experimental evidence that reducing or breaking up sitting can have beneficial effects on certain cardiometabolic biomarkers [9-12]. For example, compared to uninterrupted sitting time, adding short bouts of light or moderate intensity activity every 20-30 minutes (generally over a period of one to five days), has led to improvements in resting blood pressure [13, 14], fasting and postprandial glucose [15, 16] and insulin [15, 17, 18], and some lipids [19].

In recognition of the aforementioned evidence, several countries now, in addition to having guidelines concerning physical activity, include guidelines to reduce the quantity of sedentary behaviour and/or break it up [20-22]. A variety of intervention strategies have been trialled to reduce adults' levels of sedentary behaviour, particularly in the workplace setting [23, 24]. Reviews indicate these interventions are often effective for reducing sedentary behaviour, especially workplace interventions incorporating environmental modification, ideally as part of a multicomponent intervention [23, 25-27]. What is lacking, however, is an understanding of the nature and extent of health improvements that might be obtained when intervening to reduce sedentary behaviour over longer periods and under free-living conditions. A preliminary evaluation explored this topic (in workplace interventions only) but, having occurred prior to the emergence of several large trials of sedentary behaviour interventions, did not present any meta-analyses and could draw no firm conclusions [28].

We conducted this systematic review with meta-analyses aiming to synthesise the body of evidence that examined the effectiveness on biomarkers of cardiometabolic risk of ≥ 7 day interventions that target sedentary behaviour (alone or in combination with physical activity) in free-living conditions. We reviewed the evidence on body anthropometry, indicators of blood pressure and related haemodynamics, biomarkers relevant to the metabolism of blood glucose and lipids, and inflammatory biomarkers.

2. METHODS

This study followed the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) [29] and the Meta-analysis of Observational Studies in Epidemiology (MOOSE) [30] reporting guidelines. The systematic review protocol was prospectively registered on Prospero on 22 June 2016 (CRD42016041742. Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42016041742).

2.1 Search strategy and study selection

Six electronic databases (Ovid Medline, Ovid Embase, EBM Reviews Cochrane Central, CINAHL, Scopus, Web of Science) were searched systematically from database inception to 27 August 2019 (7 March 2017; 16 February 2018; and, 27 August 2019). A research librarian (LR) conducted an initial search for studies in Medline and Embase and used an analysis of text words and subject terms to

develop the search strategies. The final searches were then executed using the appropriate specifications of each database (LR; see Supplementary Material S1). Using reference management software (Endnote™, Clarivate Analytics, Philadelphia, USA), records were compiled, duplicates were removed, and two authors (NH and PD or RC and MG) performed title and abstract screening and reviewed each full-text article was reviewed against the inclusion criteria. Discrepancies were resolved in consultation with an independent third reviewer (EW).

2.2 Inclusion and exclusion criteria

Inclusion criteria, applied hierarchically, were: 1) reported intervening on sedentary behaviour for ≥ 7 days; 2) human study; 3) participants all aged ≥ 18 years; 4) English language; 5) full-length publication; 6) reported as an outcome at least one biomarker of cardiometabolic health, specifically concerning body anthropometry, glucose metabolism, lipid metabolism, blood pressure and related haemodynamics, or inflammation (see Supplementary Material S1); and, 7) used an intervention study design (single-group pre-post intervention, parallel-group design, or crossover). To meet criterion 1), the intervention needed to target sedentary behaviour directly or indirectly with replacement of sedentary activity with an alternative (e.g., treadmill desks), increasing 'whole-of-day' activity (which includes sedentary) or increasing 'light intensity' activity (which is almost the inverse of sedentary) or similar. Studies that only mentioned intervening on 'physical activity' or exercise could increase these activities at the expense of either sedentary behaviour or light activity, and therefore did not meet criterion 1). Further inclusion criteria for the meta-analyses were: 1) a no-intervention comparison arm (usual care / conditions; attention control); and, 2) no other intervention that was likely to provide an appreciable impact on cardiometabolic biomarkers (e.g., diet). Physical activity interventions were permitted, since reducing sedentary time very likely increases some form of physical activity as a replacement. Achievement of successful sedentary behaviour change was not considered a requirement for inclusion in the meta-analyses (to avoid potentially overstating effectiveness). Meta-analyses were conducted for each biomarker reported in at least five studies.

2.3 Data extraction

All data were extracted, checked and discrepancies resolved by the review team (NH, PD, RC, EW), using standardised rules created *a priori*. The rules used for regarding extraction, contacting authors for missing or questionable data are in Supplemental Material 2. Study quality was assessed using the Risk of Bias (RoB) 2.0 tool [31].

2.4 Statistical analysis

Analyses were performed in STATA version 16 (StataCorp, Texas USA). Significance was set at $p < 0.05$ (two-tailed). Pooled effects were estimated based on intervention effects (mean between-groups difference, in units) for the end-of-intervention endpoint extracted from each intervention, with the standard errors multiplied by $\sqrt{(n+1)/2}$ whenever there were n > 1 eligible sedentary behaviour intervention arms [32]. Pooled effects were primarily estimated from random effects (Der Simonian Laird) meta-analysis models, with fixed effects results also reported, along with heterogeneity estimates (I^2 and Cochrane's Q test) in the forest plots. A range of sensitivity analyses were also performed. Since Begg's test for publication bias can be underpowered, we also reported bias-corrected estimates from Twedie and Duval's trim and fill method. Leave-one-out sensitivity analyses were performed to consider how dependent conclusions were to any individual study. Meta-regression models, which explored possible sources of heterogeneity, are reported in the manuscript whenever heterogeneity was significant ($p < 0.05$) or substantial ($I^2 > 0.25$), otherwise in supplementary material. Characteristics considered were: mean participant age, mean outcome biomarker levels at baseline, degree of intervention effectiveness for sedentary behaviour (intervention effect on overall

sedentary time in h/day), intervention duration (≤ 3 months / 3 to 6 months / > 6 months) and study quality (RoB scores). Unadjusted and age-adjusted models were reported.

3. RESULTS

3.1 Systematic Review

3.1.1 Study inclusion

Figure 1 shows the PRISMA flow diagram. In total, 23,976 articles were identified. Most were rejected at abstract screening, with 267 articles screened as full text. The criteria mostly excluded studies on the basis they were not ≥ 7 day sedentary behaviour interventions (181/218). Fifty-four studies (55 articles) were included in the systematic review [33-87].

The population, design and intervention characteristics of the studies are reported in Supplementary Table S3 and aggregated in Table 1. Collectively, the 54 studies involved 6330 participants (48% women) with *sample sizes* usually < 100 (*k*=36) and occasionally >200 (*k*= 8), ranging between 12 and 1113. *Study populations* were recruited from developed nations, mostly English-speaking (Table 1) usually from North America (*k*=20, predominantly the USA), Europe (*k*=19), Australia (*k*=10) and occasionally from Asia (*k*=4) or Africa (*k*=1). From what little and inconsistent data was reported on ethnicity, plus the study locations, we infer that most study participants were likely Caucasian or 'White' (variously defined) with a smaller number identifying as African American or African, Hispanic and Asian ethnicities. Study mean ages ranged from 23 years [74] to 71 years [51]. Typically, the studies recruited participants from the general population (*k*=26) or a population with a chronic disease risk factor (*k*=17) (generally overweight and/or obesity, occasionally in conjunction with another risk factor). Clinical conditions [36, 37, 39, 44, 48, 59, 60, 71, 72, 81, 84] were seldom targeted for recruitment; of these only some conditions were pertinent to cardiovascular health. Many studies (*k*=25) used screening to recruit participants at risk for high sedentary behaviour based on their job (e.g., office or desk-based work) and/or their reported behaviours, while 20 studies screened based on physical activity, and 11 studies screened on both behaviours.

3.1.2 Interventions

The 54 studies delivered 56 *sedentary behaviour interventions*, mostly in the workplace (*k*=27) or community (*k*=18) settings, with healthcare (*k*=9), domestic (*k*=1) and educational settings (*k*=1) being less common (Table 1, details in Supplementary Table S3). Workplace interventions were about half multicomponent (*k*=13) and half single component (*k*=14), while interventions in the remaining non-workplace settings were mostly multicomponent (*k*=21, 72%). Workplace interventions almost all used environmental modification (*k*=26), commonly used counselling/education (*k*=13), sometimes used device self-monitoring (*k*=5), device-based social comparison (*k*=3), prompting via devices or SMS (*k*=6), and structured activity sessions (*k*=2). By contrast, non-workplace interventions almost always used some form of counselling/education (*k*=29), commonly used device self-monitoring (*k*=18) and occasionally used environmental modification (*k*=8), prompting (*k*=6), structured activity (*k*=4) and financial incentives (*k*=1). The extent of education or counselling was also highly variable, ranging from brief advice to theoretically grounded behavioural counselling.

The interventions varied in how they considered *sedentary behaviour*. Diverse behaviours were promoted as replacements for sedentary behaviour: primarily standing, walking or other stepping, but also sometimes pedalling, 'incidental' exercise (likely predominantly 'light' activities), activities of moderate or greater intensity, and sometimes resistance exercise (Supplementary Table S3). Sedentary behaviour targets seldom were domain specific, referenced accumulation patterns or set quantitative

guidelines on sedentary time (Table 1). Primary outcomes included sedentary behaviour in 23 studies, biomarkers in 11, and included neither in 20, instead being unstated (*k*=6), focused on feasibility (*k*=5), or involving physical activity with or without other outcomes (*k*=9).

3.1.3 Evaluation of biomarker indicators of cardiovascular health

The biomarkers selected for review are shown in Table 2. *Biomarker outcomes* nearly always included indicators of body anthropometry (*k*=52 studies), and often included indicators of blood pressure (*k*=37), lipid metabolism (*k*=33), and glucose metabolism (*k*=31). Four studies reported on C-reactive protein [72, 73, 75, 87]. Other inflammatory markers such as TNF-α or IL-6 were not found among the reported outcomes.

Of the *anthropometric indicators*, the most commonly reported were weight (*k*=45) or BMI (*k*=39), followed by waist circumference (*k*=37). These were almost always collected objectively by staff. Body composition outcomes were collected mostly using multifrequency bioimpedance analysis (BIA; *k*=12) or reference-grade standards: dual X-ray absorptiometry (DXA; *k*=5) or body air displacement plethysmography (BADP; *k*=3). Occasionally, other methods were used (*k*=4). Studies typically reported on body fat (*k*=25) (most commonly as percentage of body weight), and occasionally fat-free, lean or muscle mass (*k*=13). Thus, fewer studies were able to assess changes to specific tissues (e.g., fat, lean tissue) or anatomical sites (e.g. truncal fat, measured in 4 studies).

Blood pressure was generally assessed with resting blood pressure (*k*=37), which was typically reported separately as systolic (*k*=37) and/or diastolic blood pressure (*k*=36) and as mean arterial pressure in two studies [57, 82] (Table 2). Usually, staff measured blood pressure, with participants reporting values from home monitors in one study [46]. Ambulatory blood pressure was not reported. Detailed biomarkers of vascular health (e.g., endothelial dysfunction, arterial stiffness) were seldom collected. One study reported on flow mediated dilatation, carotid artery intima media thickness, aortic augmentation index, and sub endocardial variability [53]. Resting heart rate was collected in three studies [62, 69, 73].

Of the *glucose metabolism indicators* (Table 2), most (*k*=27) reported on fasting glucose, with only 13 reporting fasting insulin, and 7 reporting composite indicators of beta-cell function or insulin resistance (i.e., measures from homeostatic model assessment, HOMA or HOMA-2). Seventeen studies reported on overall glucose control (HbA1c expressed in various forms), while four studies reported effects on postprandial glucose and/or insulin [54, 58, 71, 83] and none reported on c-peptide. While venous blood draws were the norm for collecting fasting values (*k*=20 studies), lower quality fingerstick capillary measures were occasionally used (*k*=7). None of the studies reported outcomes from continuous glucose monitoring.

The most commonly reported *lipid markers* were: triglycerides (*k*=32); total cholesterol (*k*=29); High-Density Lipoprotein (HDL) cholesterol (*k*=28); and, Low-Density Lipoprotein (LDL) cholesterol (*k*=24) (Table 2). These markers are reported widely in the context of cardiovascular risk. Studies occasionally reported VLDL cholesterol [69], non-LDL cholesterol [40], or cholesterol ratios [40, 42, 43, 60, 70]. Three studies reported on apolipoproteins (APOA1, APOB and their ratio [38, 70, 73]) and one reported on the diameter of various types of cholesterol [38]. None of the studies mentioned performing detailed profiling of lipid classes or subclasses.

3.1.4 Study designs

Very few studies (*k*=5) used a single-group pre-post study design (Table 1) [46, 51, 63, 69, 78]; most used two or more groups (*k*=49). Usually the additional group (or groups) facilitated testing effectiveness against a no-intervention or attention control comparison arm (*k*=44, with 39 randomised) or occasionally only allowed for comparison of alternate interventions (*k*=5, with 5

randomised) [34, 44, 50, 67, 84]. Most studies (*k*=42) intervened for six months or less (shortest = two weeks) while few (*k*=10) intervened for 12 months or longer [43, 44, 46, 59, 60, 63, 72, 73, 76, 87] (longest = 36 months). Only nine studies referred to evaluation of maintenance of effects following withdrawal of intervention or intervention contact.

3.2 Meta-Analysis

3.2.1 Study inclusion

Of the 44 controlled intervention studies, 33 studies (34 interventions) were eligible for the meta-analyses (11 studies had provided diet intervention). For the 15 biomarkers that met the inclusion criteria (Table 2), the number of studies providing data and able to be included ranged from 6 for fat mass to 25 for body weight and blood pressure, and these studies collectively represented anywhere between 724 and 2076 participants.

3.2.2 Risk of bias

Risk of bias overall is reported in Supplementary Table S6. To simplify reporting, criteria scored for groups of outcomes with similar concerns underlying their bias risk (e.g., missing data, measurement): anthropometric and blood pressure outcomes, glucose metabolism outcomes, and lipid metabolism outcomes. Overall risk of bias was high (≥ 1 criteria was 'high' risk) in 10 studies (30%), unclear (i.e., 0 'high' risk and ≥ 1 'unclear' risk) in 17 (52%) studies and 'low' (i.e., all 'low' risk) in 6 studies (18%). The most common contributor to a 'high' risk of bias rating related to the randomisation process (*k*=6, 18%) [58, 64, 68, 76, 79, 87], (i.e., use of non-random methods). Four studies were also rated as 'high' risk of bias due to deviations from intended interventions (data not analysed according to intention to treat principles [40, 58, 74, 79]), and missing outcome data [76, 79, 83, 87]. An unclear risk level was typically assigned based on inadequate reporting of randomisation (*k*=12), concerns with missing outcome data (*k*=11), and/or bias in measurement of the outcome (*k*=9). Low risk was still permitted with lack of blinding, given the context (behavioural intervention) in which allocation is impossible to conceal from participants and is generally known to staff, and in which outcomes are collected objectively.

3.2.3 Effectiveness of sedentary behaviour interventions for biomarker outcomes

Effects on biomarkers were evaluated in the context of interventions that had displayed overall sedentary time improvements net of control that were mostly moderate (*k*=12, 30 to < 60 min/day), otherwise strong (*k*=9, ≥ 60 min/day) or small (15 to < 30 min/day, *k*=8), or occasionally almost zero (*k*=3, -15 to < 15 min/day). Effects ranged from +11.3 to -132 min/day (see Supplementary Table S4). Table 4 shows the pooled effects on biomarkers for the main analyses and sensitivity analyses. Begg's tests were all $p \geq 0.05$ (Supplementary Table S7).

Body weight and body composition

Consistent with the studies' selection criteria, prior to intervention, participants had a weighted mean (± Pooled SD) BMI of 25.4 ± 3.2 kg/m^2, with study means ranging from 22.1 kg/m^2 in a workplace intervention with no weight screening criteria [68] to 35.9 kg/m^2 in a treadmill intervention for overweight/obese office workers [56]. Baseline anthropometric values are summarised in Table 3 (detail in Supplementary Table S4). Pooled effects showed that the sedentary behaviour interventions tended to provide small improvements (net of control) in body anthropometry outcomes (Table 4). Significant pooled effects in favour of intervention were seen regarding body weight (-0.56 kg, 95% CI: -0.94, -0.17), waist circumference (-0.72 cm, 95% CI: -1.21, -0.22), body fat percentage (-0.26 %,

95% CI: -0.50, -0.02), with a tendency towards reduced fat mass (-0.33 kg, 95% CI: -0.74, 0.08) and no large or significant effect on fat-free mass (0.00 kg, 95% CI: -0.52, 0.53). Effects on BMI were in a similar direction to those for body weight, but not statistically significant (-0.07 kg/m^2, 95% CI: -0.16, 0.03). Forest plots for body weight and body composition are shown in Supplementary Figures 1 to 6. Small-study effects did not lead to overstated findings, as the original findings were no more favourable than the trimmed and filled results. Also, no single study seemed to overly influence the conclusions, as improvements observed were always still present to some degree in the leave-one-out sensitivity analyses.

Body weight and body fat percentage showed little evidence of heterogeneity ($I^2 < 25\%$; $p \geq 0.05$) with slightly more substantial (but non-significant) heterogeneity seen for fat mass and significant heterogeneity seen for waist circumference and fat-free mass. The heterogeneity in effects on fat-free mass was completely attenuated ($I^2 = 0.0$, $p = 0.790$) by omitting a single study [45]. Omission of this same study partially attenuated heterogeneity in effects on waist circumference ($I^2 = 19.9\%$, $p=0.217$). Further exploration of the heterogeneity via meta-regression (Table 5) did not show any significant predictors of effects on waist circumference. The largest effects and the smallest residual heterogeneity were seen for risk of bias scores (residual $I^2 = 22.6\%$, $p = 0.192$), with effects stronger by just over 1 cm in studies with high versus low risk of bias. Meta-regression results for the outcomes not displaying substantial or significant heterogeneity are shown in Supplementary Table S8.

Blood pressure

Prior to intervention, participants had a weighted mean (± Pooled SD) blood pressure of 110.0 ± 10.5 mmHg systolic and 78.4 ± 7.1 mmHg diastolic, indicating typically healthy levels, though with some studies attracting samples with average systolic blood pressure as high as 140 mmHg or higher [55, 70] (Table 3 and Supplementary Table S4). Pooled effects showed a small significant reduction in systolic blood pressure (-1.05 mmHg, 95% CI: -2.08, -0.02) and a smaller non-significant reduction in diastolic blood pressure (-0.69 mmHg, 95% CI: -1.69, 0.32; Table 4). Forest plots are shown in Supplementary Figures 7 and 8. Corrections for small-study effects had no effect on the results and pooled effects consistently reflected tendencies towards reduced blood pressure in the leave-one-out sensitivity analyses. Heterogeneity was minimal for systolic blood pressure ($I^2 = 8.6$, $p = 0.341$) but extensive for diastolic blood pressure ($I^2 = 52.6$, $p=0.001$), and not explained by any single study. None of the variables in the meta-regressions (Table 5) had significant associations with diastolic blood pressure or reduced the heterogeneity appreciably (residual $I^2 > 50$).

Glucose metabolism

Prior to intervention, fasting glucose averaged 4.7 ± 1.0 mM, indicating levels consistent with healthy metabolism or pre-diabetes rather than diabetes. However, the studies covered a diverse spectrum from 4.1 mM in a study of healthy adults [83] to 7.6 mM in a study of type 2 diabetes patients aged 40–80 years [72]. Baseline insulin and HbA1c levels averaged 51.5 ± 44.1 pM and 4.4 ± 0.6% were also quite variable across studies (Table 3 and Supplementary Table S5). Pooled effects pointed to small benefits to glucose metabolism, which were statistically significant only for fasting insulin (-1.42 pM, 95% CI: -2.82, -0.02) and small non-significant tendencies towards lower fasting glucose (-0.03 mM, 95% CI: -0.11, 0.05) and HbA1c (-0.10 %, 95% CI: -0.22, 0.03). Forest plots are shown in Supplementary Figures 9 to 11. Small-study effects may have overstated effects on insulin and HbA1c.

Glucose, insulin, and HbA1c all showed substantial heterogeneity ($I^2 = 45.5$ for glucose to $I^2 = 72.9$ for insulin; $p < 0.05$), which remained present in all the leave-one-out sensitivity analyses, except for glucose, where removing a single workplace study [49] that had failed to elicit changes in sedentary

behaviour markedly attenuated the heterogeneity (I^2 = 28.4, p = 0.126). Insulin outcomes were significantly beneficially associated with lower baseline levels, shorter intervention duration, and higher risk of bias, with limited residual heterogeneity after accounting for risk of bias (I^2 = 11.9, p = 0.338); however only the association with baseline level remained significant accounting for age (residual I^2 = 0.0, p = 0.641). Higher participant age significantly predicted enhanced HbA1c outcomes, and led to lower heterogeneity (residual I^2 = 49.5, p = 0.054) while in age-adjusted models, effects were significantly beneficially associated with higher BMI, longer intervention duration and lower risk of bias, and a borderline association with higher baseline levels. The model with age and BMI had no residual heterogeneity (I^2 = 0.0, p = 0.454).

Lipid metabolism

Prior to intervention, baseline levels averaged 4.3 ± 0.6 mM total cholesterol, 1.2 ± 0.4 mM HDL, 2.5 ± 0.8 mM LDL and 1.1 ± 0.5 mM triglycerides, with comparatively limited variation across studies relative to other biomarkers (Table 3 and Supplementary Table S5). Small significant improvements in response to sedentary behaviour interventions were seen in HDL cholesterol (0.04 mM, 95% CI: 0.02, 0.07) alongside a small, non-significant improvement in total cholesterol (-0.06 mM, 95% CI: -0.16, 0.04) and very small, non-significant effects on LDL cholesterol (-0.02 mM, 95% CI: -0.07, 0.04), and triglycerides (-0.02 mM, 95% CI: -0.09, 0.04). Forest plots for cholesterol and triglycerides are shown in Supplementary Figures 12 to 15. Small study effects if anything limited the effects seen for lipid metabolism, with trimmed-and-filled estimates all either larger or virtually unchanged, and with a significant effect on total cholesterol emerging (-0.10 mM, 95% CI: -0.20, -0.00).

There was limited heterogeneity in outcomes concerning HDL and LDL cholesterol (I^2 < 25, p ≥ 0.05) and more substantial and significant heterogeneity in total cholesterol (I^2 = 54.1, p=0.001) and triglycerides (I^2 = 49.0, p=0.005). Removing one study [36] markedly lowered the total cholesterol heterogeneity (I^2 = 21.1, p = 0.183) while the same was not the case for triglycerides. Meta-regressions (Table 5) showed significantly greater reductions in total cholesterol were seen with higher age, and higher risk of bias, with limited residual heterogeneity left after accounting for age (I^2 = 17.1, p=0.233) while in age-adjusted models, significant predictors of greater reductions were shorter study duration and higher risk of bias. It appears multiple factors may have contributed to the heterogeneity in triglyceride outcomes. None of the variables significantly predicted effects on triglycerides and residual heterogeneity remained high in all models (Residual I^2 =45.1–53.6). In age-adjusted models, less effectiveness in improving sedentary behaviour outcomes significantly predicted greater reductions in triglycerides (-0.13 mM, 95% CI: -0.21, -0.05), with very limited heterogeneity left when considering both these factors simultaneously (I^2 = 0.0, p=0.507), which also involved excluding one study [74] due to missing data.

4. DISCUSSION

Several reviews have reported on sedentary behaviour interventions in relation to sedentary behaviour outcomes [23, 26, 27] and found them to be effective, to varying degrees. These reviews indicated success seemed to vary depending on factors including the focus on sedentary behaviour (alone versus in combination with other lifestyle behaviours) and the type of intervention (with multicomponent workplace interventions being particularly successful). The current systematic review with meta-analyses considered these interventions in the context of their effect on biomarkers of cardiometabolic health, finding a small body of evidence. In total, 54 studies were identified, with 33 eligible for the meta-analyses, and with 6 to 25 controlled interventions ultimately included in meta-analyses concerning body anthropometry, blood pressure and haemodynamics, glucose metabolism, and lipid metabolism.

Broadly, the *meta-analyses* provided some support for small improvements in selected indicators of body anthropometry, blood pressure, glucose metabolism and lipid metabolism with intervention, with none of the outcomes tending to worsen with intervention. Specifically, significant improvements were seen in body weight, waist circumference, percentage body fat, systolic blood pressure, insulin and HDL cholesterol. For some outcomes, findings varied widely from study to study, while for others they were quite consistent, with heterogeneity ranging widely (I^2 = 0.0 to 72.9). It may be the case that some types of interventions are effective (and others ineffective), and/or the interventions may be effective in some populations but not others. The sensitivity analyses and *meta-regressions* provided some insight into potential factors underlying some of the heterogeneous results. Sometimes a single study deviating from the general pattern appeared to be the issue, while other key factors (different for each outcome) tended to be due to participant age and BMI, study duration and risk of bias. There were very few studies with each characteristic; consequently, the confidence intervals around effects were quite wide, and findings should not be taken to indicate non-significant predictors in the meta-regressions were unimportant. The low number of studies was also the reason stratified analyses were not performed to inform the effectiveness of specific types of interventions, for specific populations (e.g., men, women, older adults, and those with clinical conditions such as type 2 diabetes). Some potential success factors not able to be explored were ethnicity (poorly reported), sex, behaviour settings and dose-response. Prior findings have sometimes suggested the biological responses to sedentary time may vary depending on the setting or context in which it occurs [88, 89], by ethnicity [90-92], by sex [18, 91, 93, 94], and by the activity replacing sedentary time [95-98].

The *systematic review* showed some key considerations for interpreting the effectiveness findings. The sedentary behaviour interventions performed were highly varied in terms of their setting, use of behaviour change components, and the degree of emphasis on sedentary behaviour; thus, the heterogeneous outcomes were not highly surprising. Also, some caution should be exerted in extrapolating findings to groups with limited or no representation in the evidence base. Evidence has mostly been collected from studies of Caucasian or 'White' populations (variously defined) of working age, often with overweight/obese BMI or waist circumference, with very limited representation of those with clinical conditions pertinent to cardiovascular health, such as type 2 diabetes. The short duration of most interventions may have influenced the degree of effectiveness observed in the meta-analyses; there was a paucity of studies intervening ≥ 12 months and including maintenance evaluations from which to consider sustainability or determine what may happen in the longer term. Previously, it has been reported that biomarker results have been more promising at 12 months compared to 3 months, despite sitting reduction being greatest at 3 months [43].

To overcome the limitations of the current evidence the next logical step would be individual patient data meta-analysis, with interventions collecting 'dose' data regarding sedentary behaviour and the activities that may replace it in the most harmonisable way possible, even if this is only possible in a subsample of participants. Ideally, the measurement should allow both calculation of some total dose (e.g., in MET-hours), as well as partial out time spent sedentary and in various alternative behaviours, delineated by intensity, posture and accumulation method (e.g., sedentary/sitting, standing, light movement, moderate movement, vigorous movement, and bouted versus non-bouted forms of the relevant behaviours). Such an approach may help to determine the populations for which each intervention may be effective, as well as ascertain which specific behaviours (if any) may achieve the greatest biomarker improvements.

Other key features identified within the current evidence base are the type, reporting (or lack thereof) and specificity/sensitivity of biomarkers outcomes collected. For example, most of the biomarkers collected (e.g., blood glucose, insulin, triglycerides and blood pressure) are subject to homeostatic regulation but were only measured in fasted or resting states. It is important to also evaluate how

some sensitive biomarkers (without these limitations) that have fairly consistently responded beneficially in acute laboratory interventions lasting < 7 days [9, 11, 12, 99] respond over longer intervention timeframes. Specifically, postprandial glucose, insulin, triglycerides and ambulatory blood pressure should be measured. Other understudied outcomes that are potentially useful to measure are: detailed markers of vascular haemodynamics and structure (e.g., cardiovascular and cerebrovascular blood flow, flow-mediated dilatation and arterial stiffness) [99, 100]; C-peptide; continuous glucose monitoring; postprandial lipids; lipid subclasses [101, 102]; site-specific tissue samples (e.g., muscle, adipose tissue); and, additional intermediate biomarkers (such as those related to systemic metabolic/oxidative stress and inflammation)[9, 100]. These outcomes could be collected in all participants or in subsamples as they represent opportunities to detect changes that might otherwise be missed and improve our understanding of shared risk factors and potential mechanistic pathways.

There were some caveats regarding the overall quality of the evidence. Trimmed and filled results mostly suggested publication bias did not affect findings, but the insulin finding may be overstated and some of the lipid findings understated. Inferences were sometimes made from a very small number of studies (especially regarding biomarkers of glucose and lipid metabolism), which is especially concerning with the findings varying so much between studies. The paucity of 'low' risk of bias studies is a limitation, though importantly most studies had an 'unclear' rather than a 'high' risk of bias and the meta-regressions did not usually show high risk of bias equated to the most promising results (if anything, findings showed the opposite).

5. CONCLUSIONS

This systematic review with meta-analyses synthesised the body of work concerning the effectiveness of sedentary behaviour interventions on biomarkers of cardiometabolic risk, specifically: body anthropometry; blood pressure and related haemodynamics; glucose metabolism; lipid metabolism; and, inflammation. Consistent with evidence from prior observational research and acute laboratory-based experiments (< 7 days) linking sedentary behaviour with cardiometabolic health [8, 11, 12], the evidence from ≥7 day interventions in free-living conditions showed small improvements in some cardiometabolic biomarkers. These biomarker improvements definitively occurred in response to interventions targeting sedentary behaviour (alone or alongside physical activity), but how they occurred in response to sedentary reductions and increases in various forms of physical activity remains unknown. Our review indicated that studies in clinical populations, ethnicities other than Caucasian or 'White' in predominantly Western countries, and evaluation of biomarkers of inflammation and postprandial metabolism are key areas for future research.

COMPLIANCE WITH ETHICAL STANDARDS

Contributors

All authors reviewed the systematic review strategy. LR executed the searches. PD, NH, RC, MG and EW conducted the review and screened the initial results using standardised rules created *a priori*. PD, NH, RC and EW appraised the studies and extracted data from the primary studies and EW analysed the penultimate results. PD, NH and EW drafted the manuscript and all authors contributed to the critical revision of the manuscript and approved the final revised version. PD is the guarantor.

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Conflict of Interest

Nyssa Hadgraft, Elisabeth Winkler, Rachel Climie, Megan Grace, Lorena Romero, Neville Owen, David Dunstan, Genevieve Healy, and Paddy Dempsey declare that they have no conflicts of interest relevant to the content of this review.

REFERENCES

1. Roth GA, Johnson C, Abajobir A, *et al.* Global, Regional, and National Burden of Cardiovascular Diseases for 10 Causes, 1990 to 2015. *J Am Coll Cardiol* 2017;70:1-25.
2. GBD Disease Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1789-858.
3. Cho NH, Shaw JE, Karuranga S, *et al.* IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes research and clinical practice* 2018;138:271-81.
4. Tremblay MS, Aubert S, Barnes JD, *et al.* Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act* 2017;14:75.
5. Lynch BM, Mahmood S, Boyle T. Sedentary Behaviour and Cancer. In: Leitzmann MF, Jochem C, Schmid D, editors. Sedentary Behaviour Epidemiology. Springer Series on Epidemiology and Public Health. Cham: Springer International Publishing; 2018. p. 245-98.
6. de Rezende LF, Rodrigues Lopes M, Rey-Lopez JP, *et al.* Sedentary behavior and health outcomes: an overview of systematic reviews. *PLoS One* 2014;9:e105620.
7. Brocklebank LA, Falconer CL, Page AS, *et al.* Accelerometer-measured sedentary time and cardiometabolic biomarkers: A systematic review. *Prev Med* 2015;76:92-102.
8. Chastin SF, Egerton T, Leask C, *et al.* Meta-analysis of the relationship between breaks in sedentary behavior and cardiometabolic health. *Obesity* 2015;23:1800-10.
9. Dempsey PC, Owen N, Yates TE, *et al.* Sitting Less and Moving More: Improved Glycaemic Control for Type 2 Diabetes Prevention and Management. *Curr Diab Rep* 2016;16:114.
10. Benatti FB, Ried-Larsen M. The Effects of Breaking up Prolonged Sitting Time: A Review of Experimental Studies. *Med Sci Sports Exerc* 2015;47:2053-61.
11. Saunders TJ, Atkinson HF, Burr J, *et al.* The Acute Metabolic and Vascular Impact of Interrupting Prolonged Sitting: A Systematic Review and Meta-Analysis. *Sports Med* 2018;48:2347-66.
12. Loh R, Stamatakis E, Folkerts D, *et al.* Effects of Interrupting Prolonged Sitting with Physical Activity Breaks on Blood Glucose, Insulin and Triacylglycerol Measures: A Systematic Review and Meta-analysis. *Sports Med* 2020;50:295-330.
13. Larsen RN, Kingwell BA, Sethi P, *et al.* Breaking up prolonged sitting reduces resting blood pressure in overweight/obese adults. *Nutr Metab Cardiovasc Dis* 2014;24:976-82.
14. Dempsey PC, Sacre JW, Larsen RN, *et al.* Interrupting prolonged sitting with brief bouts of light walking or simple resistance activities reduces resting blood pressure and plasma noradrenaline in type 2 diabetes. *J Hypertens* 2016;34:2376-82.
15. Dunstan DW, Kingwell BA, Larsen R, *et al.* Breaking up prolonged sitting reduces postprandial glucose and insulin responses. *Diabetes Care* 2012;35:976-83.
16. Dempsey PC, Blankenship JM, Larsen RN, *et al.* Interrupting prolonged sitting in type 2 diabetes: nocturnal persistence of improved glycaemic control. *Diabetologia* 2017;60:499-507.
17. Henson J, Davies MJ, Bodicoat DH, *et al.* Breaking Up Prolonged Sitting With Standing or Walking Attenuates the Postprandial Metabolic Response in Postmenopausal Women: A Randomized Acute Study. *Diabetes Care* 2016;39:130-8.

18. Dempsey PC, Larsen RN, Sethi P, *et al.* Benefits for Type 2 Diabetes of Interrupting Prolonged Sitting With Brief Bouts of Light Walking or Simple Resistance Activities. *Diabetes Care* 2016;39:964-72.
19. Duvivier B, Bolijn JE, Koster A, *et al.* Reducing sitting time versus adding exercise: differential effects on biomarkers of endothelial dysfunction and metabolic risk. *Sci Rep* 2018;8:8657.
20. Piercy KL, Troiano RP, Ballard RM, *et al.* The Physical Activity Guidelines for Americans. *Jama* 2018;320:2020-8.
21. Brown WJ, Bauman AE, Bull FC, *et al.* Development of evidence-based physical activity recommendations for adults (18-64 years). Report prepared for the Australian Government Department of Health. 2012.
22. UK Chief Medical Officers' Physical Activity Guidelines. Department of Health and Social Care, Llwodraeth Cymru Welsh Government, Department of Health Northern Ireland and the Scottish Government: https://www.gov.uk/government/publications/physical-activity-guidelines-uk-chief-medical-officers-report; 2019.
23. Martin A, Fitzsimons C, Jepson R, *et al.* Interventions with potential to reduce sedentary time in adults: systematic review and meta-analysis. *Br J Sports Med* 2015;49:1056-63.
24. Shrestha N, Kukkonen-Harjula KT, Verbeek JH, *et al.* Workplace interventions for reducing sitting at work. *Cochrane Database Syst Rev* 2018;6:CD010912.
25. Chu AH, Ng SH, Tan CS, *et al.* A systematic review and meta-analysis of workplace intervention strategies to reduce sedentary time in white-collar workers. *Obes Rev* 2016;17:467-81.
26. Peachey MM, Richardson J, A VT, *et al.* Environmental, behavioural and multicomponent interventions to reduce adults' sitting time: a systematic review and meta-analysis. *Br J Sports Med* 2018.
27. Prince SA, Saunders TJ, Gresty K, *et al.* A comparison of the effectiveness of physical activity and sedentary behaviour interventions in reducing sedentary time in adults: a systematic review and meta-analysis of controlled trials. *Obes Rev* 2014;15:905-19.
28. Neuhaus M, Eakin EG, Straker L, *et al.* Reducing occupational sedentary time: a systematic review and meta-analysis of evidence on activity-permissive workstations. *Obes Rev* 2014;15:822-38.
29. Liberati A, Altman DG, Tetzlaff J, *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration2009 2009-07-21 10:46:49.
30. Stroup DF, Berlin JA, Morton SC, *et al.* Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *Jama* 2000;283:2008-12.
31. Higgins J, Sterne J, Savović J, *et al.* A revised tool for assessing risk of bias in randomized trials. 2016. In: Cochrane Methods [Internet]. : Cochrane Database of Systematic Reviews.
32. Cates C. Multiple-arm trial data: using a corrected standard error for GIV analyses. *Cochrane Colloquium* 2015;Suppl 1-327.
33. van der Pligt P, Ball K, Hesketh KD, *et al.* A pilot intervention to reduce postpartum weight retention and central adiposity in first-time mothers: results from the mums OnLiNE (Online, Lifestyle, Nutrition & Exercise) study. *J Hum Nutr Diet* 2018;31:314-28.
34. Overgaard K, Nannerup K, Lunen MKB, *et al.* Exercise more or sit less? A randomized trial assessing the feasibility of two advice-based interventions in obese inactive adults. *J Sci Med Sport* 2018;21:708-13.
35. Yang YP, Wang CJ, Wang JJ, *et al.* The Effects of an Activity Promotion System on active living in overweight subjects with metabolic abnormalities. *Obes Res Clin Pract* 2017;11:718-27.
36. Thomsen T, Aadahl M, Beyer N, *et al.* The efficacy of motivational counselling and SMS reminders on daily sitting time in patients with rheumatoid arthritis: a randomised controlled trial. *Ann Rheum Dis* 2017;76:1603-6.
37. Reeves M, Winkler E, McCarthy N, *et al.* The Living Well after Breast Cancer Pilot Trial: a weight loss intervention for women following treatment for breast cancer. *Asia Pac J Clin Oncol* 2017;13:125-36.
38. Pesola AJ, Laukkanen A, Heikkinen R, *et al.* Accelerometer-assessed sedentary work, leisure time and cardio-metabolic biomarkers during one year: Effectiveness of a cluster randomized controlled trial in parents with a sedentary occupation and young children. *PLoS One* 2017;12:e0183299.

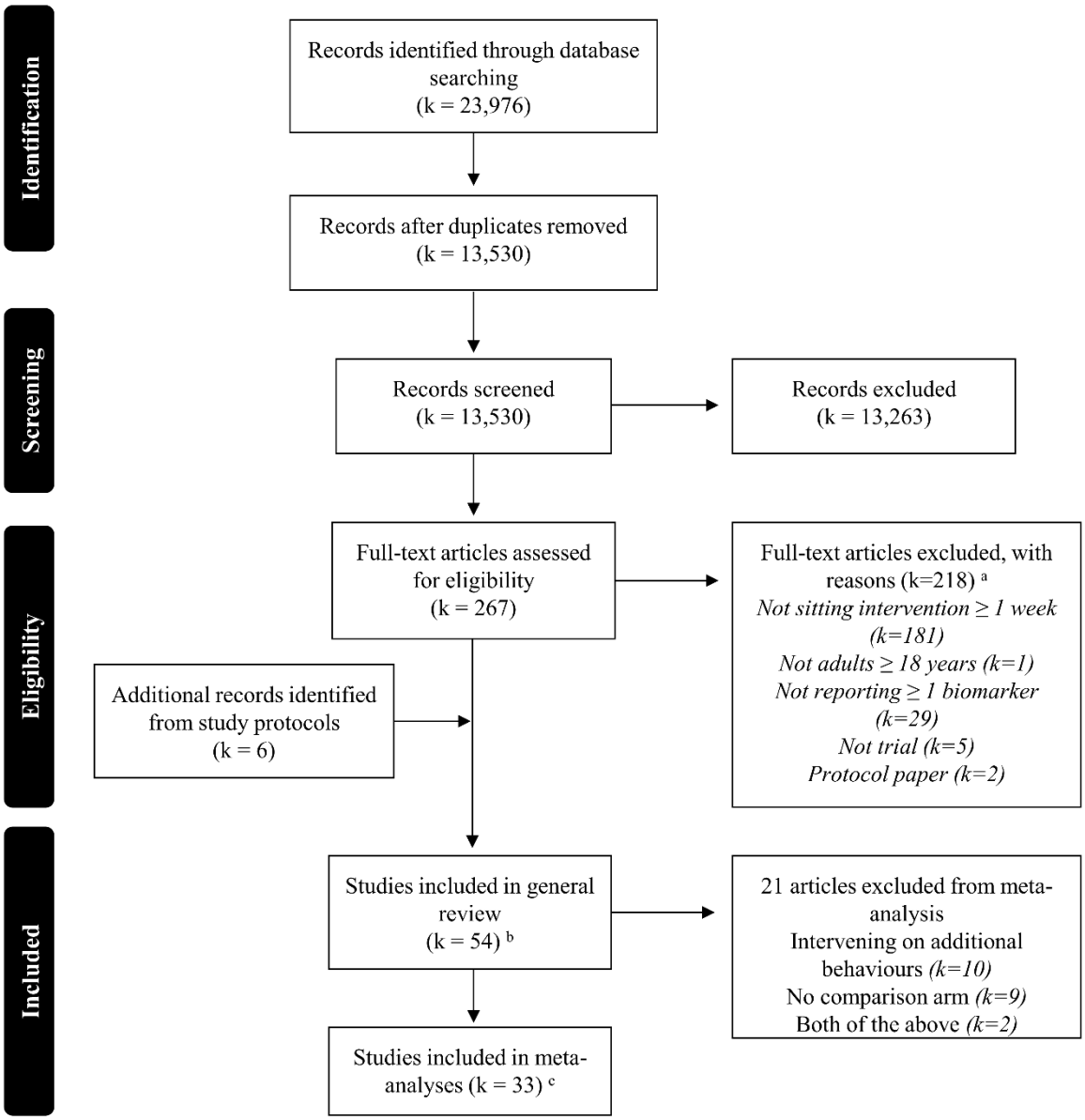
39. Miyamoto T, Fukuda K, Oshima Y, *et al.* Non-locomotive physical activity intervention using a tri-axial accelerometer reduces sedentary time in type 2 diabetes. *Phys Sportsmed* 2017;45:245-51.
40. MacEwen BT, Saunders TJ, MacDonald DJ, *et al.* Sit-Stand Desks To Reduce Workplace Sitting Time In Office Workers With Abdominal Obesity: A Randomized Controlled Trial. *J Phys Act Health* 2017;14:710-5.
41. Lyons EJ, Swartz MC, Lewis ZH, *et al.* Feasibility and Acceptability of a Wearable Technology Physical Activity Intervention With Telephone Counseling for Mid-Aged and Older Adults: A Randomized Controlled Pilot Trial. *JMIR Mhealth Uhealth* 2017;5:e28.
42. Lin YP, Lin CC, Chen MM, *et al.* Short-Term Efficacy of a "Sit Less, Walk More" Workplace Intervention on Improving Cardiometabolic Health and Work Productivity in Office Workers. *J Occup Environ Med* 2017;59:327-34.
43. Healy GN, Winkler EAH, Eakin EG, *et al.* A Cluster RCT to Reduce Workers' Sitting Time: Impact on Cardiometabolic Biomarkers. *Med Sci Sports Exerc* 2017;49:2032-9.
44. Harris L, Hankey C, Jones N, *et al.* A cluster randomised control trial of a multi-component weight management programme for adults with intellectual disabilities and obesity. *Br J Nutr* 2017;118:229-40.
45. Danquah IH, Kloster S, Holtermann A, *et al.* Take a Stand!-a multi-component intervention aimed at reducing sitting time among office workers-a cluster randomized trial. *Int J Epidemiol* 2017;46:128-40.
46. Ball K, Hunter RF, Maple JL, *et al.* Can an incentive-based intervention increase physical activity and reduce sitting among adults? the ACHIEVE (Active Choices IncEntiVE) feasibility study. *Int J Behav Nutr Phys Act* 2017;14:35.
47. Balducci S, D'Errico V, Haxhi J, *et al.* Effect of a Behavioral Intervention Strategy for Adoption and Maintenance of a Physically Active Lifestyle: The Italian Diabetes and Exercise Study 2 (IDES_2): A Randomized Controlled Trial. *Diabetes Care* 2017;40:1444-52.
48. Thomsen T, Aadahl M, Beyer N, *et al.* Motivational counselling and SMS-reminders for reduction of daily sitting time in patients with rheumatoid arthritis: a descriptive randomised controlled feasibility study. *BMC Musculoskelet Disord* 2016;17:434.
49. Taylor WC, Paxton RJ, Shegog R, *et al.* Impact of Booster Breaks and Computer Prompts on Physical Activity and Sedentary Behavior Among Desk-Based Workers: A Cluster-Randomized Controlled Trial. *Prev Chronic Dis* 2016;13:E155.
50. Mailey EL, Rosenkranz SK, Casey K, *et al.* Comparing the effects of two different break strategies on occupational sedentary behavior in a real world setting: A randomized trial. *Prev Med Rep* 2016;4:423-8.
51. Rosenberg DE, Gell NM, Jones SM, *et al.* The Feasibility of Reducing Sitting Time in Overweight and Obese Older Adults. *Health Educ Behav* 2015;42:669-76.
52. Puig-Ribera A, Bort-Roig J, Gonzalez-Suarez AM, *et al.* Patterns of impact resulting from a 'sit less, move more' web-based program in sedentary office employees. *PLoS One* 2015;10:e0122474.
53. L EFG, R CM, Shepherd SO, *et al.* Evaluation of sit-stand workstations in an office setting: a randomised controlled trial. *BMC Public Health* 2015;15:1145.
54. Biddle SJ, Edwardson CL, Wilmot EG, *et al.* A Randomised Controlled Trial to Reduce Sedentary Time in Young Adults at Risk of Type 2 Diabetes Mellitus: Project STAND (Sedentary Time ANd Diabetes). *PLoS One* 2015;10:e0143398.
55. Ashe MC, Winters M, Hoppmann CA, *et al.* "Not just another walking program": Everyday Activity Supports You (EASY) model-a randomized pilot study for a parallel randomized controlled trial. *Pilot Feasibility Stud* 2015;1:4.
56. Schuna JM, Jr., Swift DL, Hendrick CA, *et al.* Evaluation of a workplace treadmill desk intervention: a randomized controlled trial. *J Occup Environ Med* 2014;56:1266-76.
57. Mainsbridge CP, Cooley PD, Fraser SP, *et al.* The effect of an e-health intervention designed to reduce prolonged occupational sitting on mean arterial pressure. *J Occup Environ Med* 2014;56:1189-94.
58. Kozey Keadle S, Lyden K, Staudenmayer J, *et al.* The independent and combined effects of exercise training and reducing sedentary behavior on cardiometabolic risk factors. *Appl Physiol Nutr Metab* 2014;39:770-80.

59. Igelstrom H, Emtner M, Lindberg E, *et al.* Tailored behavioral medicine intervention for enhanced physical activity and healthy eating in patients with obstructive sleep apnea syndrome and overweight. *Sleep Breath* 2014;18:655-68.
60. Eakin EG, Winkler EA, Dunstan DW, *et al.* Living well with diabetes: 24-month outcomes from a randomized trial of telephone-delivered weight loss and physical activity intervention to improve glycemic control. *Diabetes Care* 2014;37:2177-85.
61. Aadahl M, Linneberg A, Moller TC, *et al.* Motivational counseling to reduce sitting time: a community-based randomized controlled trial in adults. *Am J Prev Med* 2014;47:576-86.
62. Morgan PJ, Callister R, Collins CE, *et al.* The SHED-IT community trial: a randomized controlled trial of internet- and paper-based weight loss programs tailored for overweight and obese men. *Ann Behav Med* 2013;45:139-52.
63. Koepp GA, Manohar CU, McCrady-Spitzer SK, *et al.* Treadmill desks: A 1-year prospective trial. *Obesity (Silver Spring)* 2013;21:705-11.
64. Healy GN, Eakin EG, Lamontagne AD, *et al.* Reducing sitting time in office workers: short-term efficacy of a multicomponent intervention. *Prev Med* 2013;57:43-8.
65. Carr LJ, Karvinen K, Peavler M, *et al.* Multicomponent intervention to reduce daily sedentary time: a randomised controlled trial. *BMJ Open* 2013;3:e003261.
66. Verweij LM, Proper KI, Weel AN, *et al.* The application of an occupational health guideline reduces sedentary behaviour and increases fruit intake at work: results from an RCT. *Occup Environ Med* 2012;69:500-7.
67. Steeves JA, Bassett DR, Fitzhugh EC, *et al.* Can sedentary behavior be made more active? A randomized pilot study of TV commercial stepping versus walking. *Int J Behav Nutr Phys Act* 2012;9:95.
68. Alkhajah TA, Reeves MM, Eakin EG, *et al.* Sit-stand workstations: a pilot intervention to reduce office sitting time. *Am J Prev Med* 2012;43:298-303.
69. John D, Thompson DL, Raynor H, *et al.* Treadmill workstations: a worksite physical activity intervention in overweight and obese office workers. *J Phys Act Health* 2011;8:1034-43.
70. Kallings LV, Sierra Johnson J, Fisher RM, *et al.* Beneficial effects of individualized physical activity on prescription on body composition and cardiometabolic risk factors: results from a randomized controlled trial. *Eur J Cardiovasc Prev Rehabil* 2009;16:80-4.
71. Alonso-Dominguez R, Patino-Alonso MC, Sanchez-Aguadero N, *et al.* Effect of a multifactorial intervention on the increase in physical activity in subjects with type 2 diabetes mellitus: a randomized clinical trial (EMID Study). *Eur J Cardiovasc Nurs* 2019;18:399-409.
72. Balducci S, D'Errico V, Haxhi J, *et al.* Effect of a Behavioral Intervention Strategy on Sustained Change in Physical Activity and Sedentary Behavior in Patients With Type 2 Diabetes: The IDES_2 Randomized Clinical Trial. *Jama* 2019;321:880-90.
73. Bergman F, Wahlstrom V, Stomby A, *et al.* Treadmill workstations in office workers who are overweight or obese: a randomised controlled trial. *Lancet Public Health* 2018;3:e523-e35.
74. Butler KM, Ramos JS, Buchanan CA, *et al.* Can reducing sitting time in the university setting improve the cardiometabolic health of college students? *Diabetes Metab Syndr Obes* 2018;11:603-10.
75. Dunning JR, McVeigh JA, Goble D, *et al.* The Effect of Interrupting Sedentary Behavior on the Cardiometabolic Health of Adults With Sedentary Occupations: A Pilot Study. *J Occup Environ Med* 2018;60:760-7.
76. Garland E, Watts A, Doucette J, *et al.* Stand Up to Work: assessing the health impact of adjustable workstations. *International Journal of Workplace Health Management* 2018;11:85-95.
77. Gill DP, Blunt W, Boa Sorte Silva NC, *et al.* The HealtheSteps lifestyle prescription program to improve physical activity and modifiable risk factors for chronic disease: a pragmatic randomized controlled trial. *BMC Public Health* 2019;19:841.
78. Lai A, Stewart S, Wan A, *et al.* Development and feasibility of a brief Zero-time Exercise intervention to reduce sedentary behaviour and enhance physical activity: A pilot trial. *Health Soc Care Community* 2019;27:e233-e45.
79. Malaeb S, Perez-Leighton CE, Noble EE, *et al.* A "NEAT" Approach to Obesity Prevention in the Modern Work Environment. *Workplace Health Saf* 2019;67:102-10.
80. Mantzari E, Galloway C, Wijndaele K, *et al.* Impact of sit-stand desks at work on energy expenditure, sitting time and cardio-metabolic risk factors: Multiphase feasibility study with randomised controlled component. *Prev Med Rep* 2019;13:64-72.

81. Maxwell-Smith C, Hince D, Cohen PA, *et al.* A randomized controlled trial of WATAAP to promote physical activity in colorectal and endometrial cancer survivors. *Psychooncology* 2019;28:1420-9.
82. Maylor BD, Edwardson CL, Zakrzewski-Fruer JK, *et al.* Efficacy of a Multicomponent Intervention to Reduce Workplace Sitting Time in Office Workers: A Cluster Randomized Controlled Trial. *J Occup Environ Med* 2018;60:787-95.
83. Peterman JE, Morris KL, Kram R, *et al.* Cardiometabolic Effects of a Workplace Cycling Intervention. *J Phys Act Health* 2019;16:547-55.
84. Prince SA, Reed JL, Cotie LM, *et al.* Results of the Sedentary Intervention Trial in Cardiac Rehabilitation (SIT-CR Study): A pilot randomized controlled trial. *Int J Cardiol* 2018;269:317-24.
85. Resendiz M, Lustik MB, Conkright WR, *et al.* Standing desks for sedentary occupations: Assessing changes in satisfaction and health outcomes after six months of use. *Work* 2019;63:347-53.
86. Wyke S, Bunn C, Andersen E, *et al.* The effect of a programme to improve men's sedentary time and physical activity: The European Fans in Training (EuroFIT) randomised controlled trial. *PLoS Med* 2019;16:e1002736.
87. Zhu W, Gutierrez M, Toledo MJ, *et al.* Long-term effects of sit-stand workstations on workplace sitting: A natural experiment. *J Sci Med Sport* 2018;21:811-6.
88. Dempsey PC, Hadgraft NT, Winkler EAH, *et al.* Associations of context-specific sitting time with markers of cardiometabolic risk in Australian adults. *Int J Behav Nutr Phys Act* 2018;15:114.
89. Ullrich A, Voigt L, Baumann S, *et al.* A cross-sectional analysis of the associations between leisure-time sedentary behaviors and clustered cardiometabolic risk. *BMC Public Health* 2018;18:327.
90. Barone Gibbs B, Pettee Gabriel K, Carnethon MR, *et al.* Sedentary Time, Physical Activity, and Adiposity: Cross-sectional and Longitudinal Associations in CARDIA. *Am J Prev Med* 2017;53:764-71.
91. Healy GN, Matthews CE, Dunstan DW, *et al.* Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06. *Eur Heart J* 2011;32:590-7.
92. Yates T, Edwardson CL, Celis-Morales C, *et al.* Metabolic Effects of Breaking Prolonged Sitting With Standing or Light Walking in Older South Asians and White Europeans: A Randomized Acute Study. *J Gerontol A Biol Sci Med Sci* 2020;75:139-46.
93. Thorp AA, Healy GN, Owen N, *et al.* Deleterious associations of sitting time and television viewing time with cardiometabolic risk biomarkers: Australian Diabetes, Obesity and Lifestyle (AusDiab) study 2004-2005. *Diabetes Care* 2010;33:327-34.
94. Wheeler MJ, Dunstan DW, Ellis KA, *et al.* Effect of Morning Exercise With or Without Breaks in Prolonged Sitting on Blood Pressure in Older Overweight/Obese Adults. *Hypertension* 2019;73:859-67.
95. Debache I, Bergouignan A, Chaix B, *et al.* Associations of Sensor-Derived Physical Behavior with Metabolic Health: A Compositional Analysis in the Record Multisensor Study. *Int J Environ Res Public Health* 2019;16:741.
96. Healy GN, Winkler EA, Owen N, *et al.* Replacing sitting time with standing or stepping: associations with cardio-metabolic risk biomarkers. *Eur Heart J* 2015;36:2643-9.
97. Chastin SF, Palarea-Albaladejo J, Dontje ML, *et al.* Combined Effects of Time Spent in Physical Activity, Sedentary Behaviors and Sleep on Obesity and Cardio-Metabolic Health Markers: A Novel Compositional Data Analysis Approach. *PLoS One* 2015;10:e0139984.
98. Winkler EAH, Chastin S, Eakin EG, *et al.* Cardiometabolic Impact of Changing Sitting, Standing, and Stepping in the Workplace. *Med Sci Sports Exerc* 2018;50:516-24.
99. Dempsey PC, Larsen RN, Dunstan DW, *et al.* Sitting Less and Moving More: Implications for Hypertension. *Hypertension* 2018;72:1037-46.
100. Dempsey PC, Matthews CE, Dashti SG, *et al.* Sedentary Behavior and Chronic Disease: Mechanisms and Future Directions. *J Phys Act Health* 2019;17:1-10.
101. Grace MS, Dempsey PC, Sethi P, *et al.* Breaking Up Prolonged Sitting Alters the Postprandial Plasma Lipidomic Profile of Adults With Type 2 Diabetes. *J Clin Endocrinol Metab* 2017;102:1991-9.

102. O'Keefe JH, Bell DSH. Postprandial Hyperglycemia/Hyperlipidemia (Postprandial dysmetabolism) is a cardiovascular risk factor. *American Journal of Cardiology* 2007;100:899-904.

Fig. 1 PRISMA diagram of the literature search results.



[a] exclusion criteria were applied in the following order: 1) not sitting intervention ≥ 1 week, 2) not a human study, 3) not English language, 4) not full-length publication, 5) not reporting ≥ 1 biomarker, 6) not randomised, quasi-randomised or pre-post trial, 7) not adults ≥ 18 years.
[b] Two articles were identified for one study (Balducci 2017, Balducci 2019)
[c] k=32 for anthropometry measures; k=25 for blood pressure measures; k=22 for glucose measures; k=24 lipid measures; k=4 inflammatory measures.

Table 1 Summary of the study population, design and intervention characteristics of adult sedentary behaviour interventions ≥ 7 days with biomarker outcomes

Characteristic		**Count** [a]	**Detail**
Population / study characteristics (54 studies)			
Sample size	Median n/study	57	Lowest = 12, Highest = 1113
	Total n	5217	Female n=3065 (48.4%), Male n=3265 (51.6%)
Location (Continent & Country: ISO 2-digit country codes)	North America	20	USA 16, CA 4
	Europe	19	UK 5, DK 4, SE 3, ES 2, NL 1, DK & GL 1, FI 1, IT 1, UK & NL & NO & PT 1
	Australia	10	
	Asia	4	TW 2, CN 1, JP 1
	Africa	1	ZA 1
Ethnicity	>50% Caucasian / 'white'	18	
	<50% Caucasian / 'white'	2	
	Not reported	33	
Clinical population	Clinical condition	11	T2D 4, Cancer 2, Rheumatoid Arthritis 2, Obstructive Sleep Apnoea 1, Intellectual Disability 1, Coronary Artery Disease 1
	Clinical risk factors only	17	Adiposity 14, Chronic disease risk (+ adiposity) 3
	Healthy / general	26	
Screening	Sedentary job / behaviour	25	11 also screened for PA, 14 did not
	Physical activity (PA)	30	11 also screened for PA, 19 did not
Study design	Randomised Controlled Trial	39	8 cluster / 31 individually randomised 34 parallel group / 3 crossover / 1 other [b]
	Non-randomised Controlled Trial	5	1 cluster / 4 individually allocated 5 parallel group / 0 crossover
	Multi-arm (no controls)	5	1 cluster randomised / 4 individually randomised
	Pre-post (single arm)	5	
Primary Outcomes	Includes sedentary	22	
	Includes biomarker(s)	10	
	Includes both	1	
	Includes neither	21	PA 8 / PA & diet 1, Unstated 6, Feasibility, 5 Fitness
Intervention characteristics (56 interventions)			
Duration	3 months or less	28	
	>3-6 months	16	
	>6 months	12	
Setting	Workplace	27	
	Community	18	
	Other	11	Hospital 5, Primary care 4, Domestic 1, Education 1
N components	Multicomponent	34	Workplace 13, Community/Other 21
	Single component	22	Workplace 14, Community/Other 8
Components [c]	Counselling/education	41	Workplace 13, Community/Other 28
	Environmental modification	34	Workplace 26, Community/Other 8
	Prompting	12	Workplace 6, Community/Other 6
	Structured 'activity'	5	Workplace 2, Community/Other 4
	Device self-monitoring	23	Workplace 5, Community/Other 18
	Device social comparison	7	Workplace 3, Community/Other 4
	Financial incentives	2	Workplace 1, Community/Other 1
Sedentary targets / messaging [c]	Domain specific message	29	
	Accumulation	21	
	Quantitative volume target	14	

BMI = Body Mass Index; WC = Waist Circumference; PA = Physical activity

[a] count out of 54 studies or 56 interventions as indicated in the table unless other statistic is mentioned (e.g., median).

[b] almost a randomised controlled trial (parallel groups) except re-enrolled some controls into the intervention upon completion.

[c] Not mutually exclusive (interventions can have multiple components, multiple messages)

Table 2 Biomarkers reported as outcomes in 54 studies of adult sedentary behaviour interventions ≥ 7 days

Outcomes	Studies	Detail	Quality factors
Body Anthropometry	52		
Body weight [a]	45	45 weight [a], 39 body mass index [a]	Objective [b] / self-report: 44 / 1
Waist circumference [a]	37	37 circumference [a], 2 waist-hip ratio	Objective [b] / self-report: 36 / 1
Other body measurements	9	7 hip circumference, 1 neck circumference, 2 sagittal abdominal diameter	
Body composition	25		BIA: 12 DXA: 5 BIS: 2 BADP: 3 Skinfold(s): 2 Unreported: 1
-Total fat	25	20 percentage of body weight [a], 11 mass [a]	
-Total fat-free or lean	13	12 percentage of body weight, 1 mass [a],	
-Other	5	fat mass or % (4 truncal, 1 arm, 1 leg, 1 android %, 1 gynoid %); fat-free mass or % (1 arm, 1 leg); 1 skeletal muscle mass; 1 visceral fat area	
Blood Pressure (BP) Regulation	37		
Resting BP [a]	37	37 systolic [a], 36 diastolic [a] 2 mean arterial BP	Objective [b] / self-report: 36 / 1
Ambulatory BP	0	-	-
Heart rate	5	3 resting, 2 non-resting	Objective [b] / self-report: 5 / 0
Detailed vascular health measures	3	1 flow mediated dilation, 1 carotid intima media thickness, 1 aortic augmentation index, 1 subendocardial variability, 1 pulse wave velocity	Objective [b] / self-report: 3 / 0
Glucose Metabolism	31		
Fasting glucose [a]	27		Venous / Capillary: 20 / 7
Fasting insulin [a]	13		
HOMA/HOMA-2	7	6 HOMA-IR, 2 HOMA-%B, 1 HOMA2-%B, 1 HOMA2-%S	
Postprandial glucose / insulin	4	4 postprandial glucose, 1 postprandial insulin, 1 Insulin AUC, 1 Glucose AUC, 1 C-ISI	Venous / Capillary: 4 / 0 Duration: all 2 h test
C-peptide	0		-
HbA1c [a]	17	15 HbA1c, 2 'estimated average glucose' reported as HbA1c	Venous / Capillary: 15 / 2
Lipid Metabolism	33		
Cholesterol levels or ratios	33	29 total [a], 28 HDL [a], 24 LDL [a], 1 VLDL, 1 non-LDL, 5 Total/HDL, 2 LDL/HDL	Venous / Capillary: 25 / 8
Triglycerides [a]	32		Fasted / Insufficient / Non-fasted state: 25 / 1 / 7
Other	3	1 Cholesterol diameter; 1 Lipoprotein Lipase; 3 Apolipoproteins (APO): 3 APO-A1, 3 APO-B, 2 APO-A1/APO-B	
Inflammation	4		
C-reactive protein (CRP)	4	2 CRP; 2 high-sensitivity CRP	Venous / Capillary: 4 / 0 Fasted / Insufficient / Non-fasted state: 4 / 0 / 0
Other: TNF-α, IL-6	0		-

HOMA = Homeostatic Model Assessment; HOMA-2 = Revised Homeostatic Model Assessment; HDL = high-density lipoprotein; LDL= low-density lipoprotein; TNF-α = tumour necrosis factor alpha; IL-6= interleukin 6. BIA = multifrequency bioimpedance analysis; DXA = dual X-ray absorptiometry; BIS = bioelectrical impedance spectroscopy; BADP = body air displacement plethysmography; AUC = area under the curve; C-ISI = composite insulin sensitivity index.

[a] Outcome included in the meta-analyses: was reported in > 5 of the 33 studies eligible for the effectiveness meta-analyses (had control arm, no additional relevant intervention provided apart from active behaviours)

[b] Measured objectively by research staff

Note. Data were extracted from the earlier paper related to this study (Balducci 2017) when it was not reported in the 2019 paper (%BF; FFM; BMI; fasting insulin; HOMA).

Table 3 Average biomarker characteristics prior to intervention in controlled trials of 34 adult sedentary behaviour interventions ≥7 days with biomarker outcomes

	k	n	Weighted mean ± pooled SD	Study means (min – max)	Study with lowest mean	Study with highest mean
Weight, kg	29	2456	71.3 ± 10.6	62.2 – 99.6	Alkhajah et al. (2012)	MacEwen et al. (2017)
Body mass index, kg/m^2	34	3186	25.4 ± 3.2	22.1 – 35.9	Alkhajah et al. (2012)	Schuna et al. (2014)
Waist circumference, cm	21	2630	83.9 ± 7.7	74.4 – 111.4	Butler et al. (2018)	MacEwen et al. (2017)
Body fat, %	18	2050	28.1 ± 5.4	24.5 – 45.5	Dunning et al. (2018)	Kozey-Keadle et al. (2014)
Fat mass, kg	7	753	25.3 ± 7.7	18.4 – 32.3	Alkhajah et al. (2012)	Kallings et al. (2009)
Fat-free mass, kg	8	1252	40.0 ± 6.7	44.1 – 56.5	Alkhajah et al. (2012)	Balducci et al. (2019)
Systolic BP, mmHg	25	2461	110.0 ± 10.5	109 – 142	Dunning et al. (2018)	Maxwell-Smith et al. (2018)
Diastolic BP, mmHg	25	2457	68.4 ± 6.5	69 – 86	Peterman et al. (2019)	MacEwen et al. (2017); Maxwell-Smith et. al (2018)
Glucose, mM	19	1975	4.7 ± 1.0	4.1 – 7.6	Peterman et al. (2019)	Balducci et al. (2019)
Insulin, pM	11	1495	51.5 ± 44.1	37.1 – 133.0	Dunning et al. (2018)	Kozey-Keadle et al. (2014)
HbA1c, %	11	1308	4.4 ± 0.6	4.9 – 7.4	Kallings et al. (2009)	Balducci et al. (2019)
Total cholesterol, mM	24	2292	4.3 ± 0.6	4.0 – 5.5	Peterman et al. (2019)	Kallings et al. (2009)
HDL cholesterol, mM	22	2232	1.2 ± 0.4	1.1 – 1.8	Peterman et al. (2019)	Pesola et al. (2017)
LDL cholesterol, mM	21	2142	2.5 ± 0.8	2.5 – 3.3	Peterman et al. (2019)	Kallings et al. (2009)
Triglycerides, mM	23	2202	1.1 ± 0.5	0.9 – 1.9	Alkhajah et al. (2012)	Kozey-Keadle et al. (2014)

k= number of interventions, n = number of participants

HDL = high-density lipoprotein; LDL= low-density lipoprotein; BP = Blood pressure

Table 4 Pooled intervention effects on biomarkers: controlled trials of 35 adult sedentary behaviour interventions ≥7 days

n

Outcome	Main findings					Publication-bias corrected	Leave-one-out sensitivity analysis	
	k	n	All studies				Most benefit	Least benefit
			I^2, *p*	Pooled effect (95% CI)	*p*	Pooled (95% CI)	Pooled effect (95% CI)	Pooled effect (95% CI)
Weight, kg	25	1839	23.6%, p=0.142	**-0.56 (-0.94, -0.17)**	**0.005**	n/a	**-0.63 (-1.03, -0.23)** [a]	**-0.47 (-0.75, -0.18)** [b]
Body Mass Index, kg/m^2	24	1843	0.0%, p=0.804	-0.07 (-0.16, 0.03)	0.167	-0.08 (-0.17, 0.02)	-0.10 (-0.20, 0.01) [c]	-0.04 (-0.14, 0.06) [d]
Waist circumference, cm	19	2076	**45.8%, p=0.016**	**-0.72 (-1.21, -0.22)**	**0.004**	**-1.00 (-1.51, -0.49)**	**-0.95 (-1.38, -0.51)**[# e]	**-0.61 (-1.20, -0.01)** [# f]
Body fat, %	16	1618	5.5%, p=0.390	**-0.26 (-0.50, -0.02)**	**0.034**	**-0.37 (-0.65, -0.10)**	**-0.37 (-0.61, -0.12)** [c]	-0.17 (-0.43, 0.09) [e]
Fat mass, kg	6	724	26.6%, p=0.235	-0.33 (-0.74, 0.08)	0.116	n/a	**-0.42 (-0.73, -0.10)** [g]	-0.23 (-0.63, 0.16) [h]
Fat-free mass, kg	7	1011	**72.7%, p=0.001**	0.00 (-0.52, 0.53)	0.992	0.48 (-0.02, 0.98)	0.12 (-0.40, 0.65) [c]	-0.25 (-0.57, 0.06) [# e]
Blood pressure, mmHg								
Systolic	25	1932	8.6%, p=0.341	**-1.05 (-2.08, -0.02)**	**0.045**	n/a	**-1.42 (-2.38, -0.45)** [c]	-0.75 (-1.81, 0.31) [i]
Diastolic	25	1932	**52.6%, p=0.001**	-0.69 (-1.69, 0.32)	0.180	n/a	-0.92 (-1.86, 0.02) [j]	-0.36 (-1.28, 0.56) [k]
Glucose, mM	19	1518	**45.5%, p=0.017**	-0.03 (-0.11, 0.05)	0.526	-0.04 (-0.13, 0.05)	-0.05 (-0.11, 0.02)[# l]	-0.01 (-0.11, 0.09) [i]
Insulin, pM	10	1102	**64.0%, p=0.003**	**-1.42 (-2.82, -0.02)**	**0.047**	-1.03 (-2.48, 0.42)	**-4.13 (-7.48, -0.78)** [m]	-0.45 (-1.60, 0.69) [#a]
HbA1c, %	9	892	**72.9%, p=0.000**	-0.10 (-0.22, 0.03)	0.129	-0.03 (-0.16, 0.09)	-0.14 (-0.29, 0.01) [n]	-0.05 (-0.17, 0.07) [h]
Cholesterol, mM								
Total	23	1798	**54.1%, p=0.001**	-0.06 (-0.16, 0.04)	0.213	**-0.10 (-0.20, -0.00)**	-0.08 (-0.18, 0.02) [l]	-0.03 (-0.11, 0.05) [#o]
High Density Lipoprotein	22	1760	22.5%, p=0.168	**0.04 (0.02, 0.07)**	**<0.001**	**0.05 (0.02, 0.07)**	**0.05 (0.03, 0.07)** [d]	**0.03 (0.01, 0.06)** [i]
Low Density Lipoprotein	20	1660	0.0%, p=0.690	-0.02 (-0.07, 0.04)	0.562	-0.01 (-0.07, 0.05)	-0.03 (-0.09, 0.03) [l]	-0.00 (-0.06, 0.06) [p]
Triglycerides, mM	23	1742	**49.0%, p=0.005**	-0.02 (-0.09, 0.04)	0.496	-0.06 (-0.13, 0.01)	-0.04 (-0.10, 0.03) [g]	-0.01 (-0.07, 0.06) [h]

k, n = number of interventions, number of individuals (sum of n analysed in each included study)
Boldface indicates pooled effect is $p < 0.05$ *Heterogeneity $p < 0.05$ # Heterogeneity no longer $p < 0.05$ in leave-one-out sensitivity analysis
[a] Omitted Healy et al. (2017) [b] Omitted Ashe et al. (2015) [c] Omitted Maylor et al. (2018) [d] Omitted Pesola et al. (2017) [e] Omitted Danquah et al. (2017) [f] Omitted Puig-Ribera et al. (2015) [g] Omitted Healy et al. (2013) [h] Omitted Kallings et al. (2017) [i] No Butler et al. (2018) [j] Omitted Mantzari et al. (2018) [k] Omitted Lin et al. (2017) [l] Omitted Taylor et al. (2016) (Computer intervention) [m] Omitted Balducci (2019) [n] Omitted Biddle (2015) [o] Omitted Thomsen et al. (2017) [p] Omitted Aadahl et al. (2014)

Table 5 Associations of study characteristics with intervention effects on cardiometabolic biomarkers (meta-regression)

	Unadjusted				Age adjusted			
	k, n	**b (95% CI)**	**p**	**I^2, p**	**n, N**	**b (95% CI)**	**p**	**I^2, p**
Waist circumference, cm	**19, 2076**			**45.8%, p=0.016**	**19, 2076**			**45.8%, p=0.016**
Mean baseline age, per 10 y	18, 2050	-0.50 (-1.18, 0.17)	0.144	51.6%, p = 0.007		-	-	-
Mean baseline BMI, kg/m^2	19, 2076	-0.04 (-0.25, 0.16)	0.672	48.6%, p = 0.011	18, 2050	-0.01 (-0.24, 0.22)	0.910	54.5%, p = 0.005
Mean baseline level	19, 2076	0.01 (-0.08, 0.09)	0.856	44.9%, p = 0.021	18, 2050	0.07 (-0.03, 0.18)	0.182	45.9%, p = 0.023
Sedentary effectiveness, h/day [c]	19, 2076	-0.62 (-1.42, 0.18)	0.127	38.7%, p = 0.048	18, 2050	-1.05 (-1.96, -0.14)	0.023	40.3%, p = 0.049
Duration (vs ≤3 months)	19, 2076		*0.896*	51.8%, p = 0.007	18, 2050		*0.307*	57.7%, p = 0.003
3–6 months		0.15 (-1.08, 1.37)	0.816			0.92 (-0.69, 2.52)	0.262	
>6 months		-0.36 (-2.28, 1.57)	0.717			-0.25 (-2.28, 1.78)	0.809	
Risk of bias (vs High risk)	19, 2076		*0.098*	22.6%, p = 0.192	18, 2050		*0.109*	25.4%, p = 0.174
Some concerns		-0.70 (-2.50, 1.09)	0.441			-0.52 (-2.39, 1.34)	0.582	
Low risk		-1.47 (-3.10, 0.16)	0.077			-1.36 (-3.03, 0.31)	0.110	
Fat-free mass, kg	**7, 1011**			**72.7%, p=0.001**	**7, 1011**			**72.7%, p=0.001**
Mean baseline age, per 10 y	7, 1011	0.14 (-0.60, 0.88)	0.714	74.5%, p = 0.001		-	-	-
Mean baseline BMI, kg/m^2	7, 1011	0.07 (-0.18, 0.32)	0.575	76.8%, p <0.001	7, 1011	0.07 (-0.24, 0.38)	0.660	79.6%, p = <0.001
Mean baseline level	7, 1011	0.04 (-0.10, 0.18)	0.540	75.0%, p = 0.001	7, 1011	0.06 (-0.16, 0.27)	0.618	79.4%, p = <0.001
Sedentary effectiveness, h/day [c]	7, 1011	0.23 (-0.98, 1.44)	0.711	77.1%, p <0.001	7, 1011	0.21 (-1.02, 1.44)	0.738	79.4%, p = <0.001
Duration (> 6vs ≤3 months) [d]	7, 1011	0.06 (-1.23, 1.36)	0.922	77.1%, p <0.001	7, 1011	-0.14 (-1.86, 1.58)	0.875	77.6%, p = 0.001
Risk of bias (vs High risk)	7, 1011		*0.490*	69.9%, p = 0.010	7, 1011		*0.619*	74.5%, p = 0.008
Some concerns		0.72 (-0.53, 1.98)	0.258			1.23 (-0.73, 3.20)	0.219	
Low risk		0.12 (-1.10, 1.34)	0.847			0.37 (-1.07, 1.81)	0.615	
Glucose, mM	**19, 1518**			**45.5%, p=0.017**	**19, 1518**			**45.5%, p=0.017**
Mean baseline age, per 10 y	19, 1518	-0.01 (-0.08, 0.07)	0.891	47.9%, p = 0.012		-	-	-
Mean baseline BMI, kg/m^2	19, 1518	0.01 (-0.01, 0.03)	0.391	46.0%, p = 0.017	19, 1518	0.01 (-0.01, 0.04)	0.330	48.8%, p = 0.012
Mean baseline level	18, 1497	-0.01 (-0.23, 0.20)	0.908	45.8%, p = 0.021	18, 1497	0.03 (-0.23, 0.29)	0.819	46.0%, p = 0.023
Sedentary effectiveness, h/day [c]	18, 1497	-0.02 (-0.21, 0.16)	0.804	45.6%, p = 0.021	18, 1497	-0.05 (-0.25, 0.15)	0.632	46.0%, p = 0.023

Duration (vs ≤3 months)	19, 1518		*0.611*	51.5%, p = 0.007	19, 1518		*0.732*	54.0%, p = 0.005
3–6 months		-0.00 (-0.19, 0.19)	0.980			0.04 (-0.24, 0.32)	0.769	
>6 months		-0.12 (-0.37, 0.13)	0.345			-0.14 (-0.43, 0.15)	0.355	
Risk of bias (vs High risk)	19, 1518		*0.424*	48.3%, p = 0.014	19, 1518		*0.543*	49.7%, p = 0.013
Some concerns		0.18 (-0.13, 0.48)	0.256			0.21 (-0.12, 0.54)	0.212	
Low risk		0.12 (-0.09, 0.33)	0.267			0.17 (-0.09, 0.42)	0.202	
Insulin, pM	**10, 1102**			**64.0%, p=0.003**	**10, 1102**			**64.0%, p=0.003**
Mean baseline age, per 10 y	10, 1102	0.76 (-2.63, 4.15)	0.660	68.0%, p = 0.002		-	-	-
Mean baseline BMI, kg/m^2	10, 1102	0.20 (-1.09, 1.48)	0.764	67.8%, p = 0.002	10, 1102	0.02 (-1.60, 1.65)	0.980	68.8%, p = 0.002
Mean baseline level	10, 1102	0.15 (0.03, 0.27)	0.018	61.1%, p = 0.008	10, 1102	0.21 (0.12, 0.31)	<0.001	0.0%, p = 0.641
Sedentary effectiveness, h/day [c]	10, 1102	1.65 (-6.15, 9.45)	0.678	66.5%, p = 0.002	10, 1102	3.51 (-6.34, 13.35)	0.485	45.4%, p = 0.077
Duration (vs ≤3 months)	10, 1102		*0.014*	50.8%, p = 0.047	10, 1102		*0.268*	57.8%, p = 0.027
3–6 months		2.14 (-7.20, 11.48)	0.654			1.87 (-8.64, 12.38)	0.728	
>6 months		7.87 (-0.21, 15.95)	0.056			6.84 (-2.33, 16.01)	0.144	
Risk of bias (vs High risk)	10, 1102		*<0.001*	11.9%, p = 0.338	10, 1102		*0.211*	22.8%, p = 0.255
Some concerns		-0.24 (-1.42, 0.94)	0.692			-3.10 (-11.81, 5.62)	0.486	
Low risk		-4.64 (-6.95, -2.32)	<0.001			-5.60 (-11.33, 0.14)	0.056	
HbA1c, %	**9, 892**			**72.9%, p=0.000**	**9, 892**			**72.9%, p=0.000**
Mean baseline age, per 10 y	9, 892	-0.10 (-0.18, -0.02)	0.011	49.5%, p = 0.054		-	-	-
Mean baseline BMI, kg/m^2	9, 892	-0.01 (-0.05, 0.03)	0.599	76.3%, p<0.001	9, 892	-0.03 (-0.05, -0.01)	0.004	0.0%, p = 0.454
Mean baseline level	9, 892	-0.15 (-0.34, 0.04)	0.127	76.3%, p <0.001	9, 892	-0.16 (-0.32, 0.00)	0.055	49.1%, p = 0.067
Sedentary effectiveness, h/day [c]	9, 892	0.08 (-0.10, 0.26)	0.379	69.5%, p = 0.002	9, 892	-0.02 (-0.20, 0.17)	0.862	56.4%, p = 0.032
Duration (vs ≤3 months)	9, 892		*0.994*	78.0%, p <0.001	9, 892		*0.002*	24.7%, p = 0.249
3–6 months		-0.02 (-0.35, 0.32)	0.919			0.04 (-0.14, 0.23)	0.641	
>6 months		-0.02 (-0.38, 0.35)	0.932			-0.24 (-0.50, 0.02)	0.069	
Risk of bias (vs High risk)	9, 892		*0.090*	75.4%, p <0.001	9, 892		*0.037*	59.4%, p = 0.031
Some concerns		0.30 (-0.25, 0.85)	0.287			0.28 (-0.23, 0.79)	0.286	
Low risk		0.50 (-0.02, 1.02)	0.058			0.40 (-0.09, 0.89)	0.113	

Diastolic Blood Pressure, mmHg	**25, 1932**			**52.6%, p=0.001**	**25, 1932**			**52.6%, p=0.001**
Mean baseline age, per 10 y	25, 1932	-0.38 (-1.30, 0.54)	0.421	54.4%, p <0.001		-	-	-
Mean baseline BMI, kg/m^2	24, 1903	-0.01 (-0.32, 0.30)	0.946	53.2%, p = 0.001	24, 1903	0.03 (-0.31, 0.36)	0.885	55.2%, p = <0.001
Mean baseline level	24, 1911	-0.16 (-0.44, 0.12)	0.250	52.0%, p = 0.002	24, 1911	-0.11 (-0.42, 0.20)	0.492	52.5%, p = 0.002
Sedentary effectiveness, h/day [c]	23, 1882	-1.07 (-2.83, 0.69)	0.232	52.9%, p = 0.002	23, 1882	-1.69 (-3.40, 0.02)	0.053	43.2%, p = 0.019
Duration (vs ≤3 months)	25, 1932		*0.655*	56.2%, p <0.001	25, 1932		*0.712*	57.9%, p = <0.001
3–6 months		0.22 (-2.50, 2.94)	0.874			0.40 (-2.64, 3.43)	0.798	
>6 months		-1.20 (-3.97, 1.57)	0.397			-1.14 (-4.19, 1.92)	0.465	
Risk of bias (vs High risk)	25, 1932		*0.699*	55.1%, p <0.001	25, 1932		*0.629*	57.1%, p = <0.001
Some concerns		1.20 (-2.05, 4.45)	0.468			1.82 (-1.90, 5.53)	0.338	
Low risk		1.03 (-1.58, 3.64)	0.439			1.35 (-1.56, 4.25)	0.363	
Total Cholesterol, mM	**23, 1798**			**54.1%, p=0.001**	**23, 1798**			**54.1%, p=0.001**
Mean baseline age, per 10 y	23, 1798	-0.14 (-0.22, -0.07)	<0.001	17.1%, p = 0.233		-	-	-
Mean baseline BMI, kg/m^2	23, 1798	0.01 (-0.02, 0.04)	0.664	54.6%, p = 0.001	23, 1798	0.01 (-0.01, 0.03)	0.398	17.4%, p = 0.233
Mean baseline level	23, 1798	-0.24 (-0.50, 0.02)	0.066	45.7%, p = 0.011	23, 1798	-0.05 (-0.30, 0.21)	0.713	20.6%, p = 0.195
Sedentary effectiveness, h/day [c]	23, 1798	0.08 (-0.04, 0.20)	0.206	40.3%, p = 0.027	23, 1798	0.01 (-0.10, 0.12)	0.812	19.5%, p = 0.208
Duration (vs ≤3 months)	23, 1798		*0.573*	54.6%, p = 0.001	23, 1798		*0.003*	20.4%, p = 0.202
3–6 months		0.07 (-0.17, 0.31)	0.577			0.06 (-0.12, 0.24)	0.493	
>6 months		0.13 (-0.12, 0.39)	0.306			0.11 (-0.08, 0.30)	0.259	
Risk of bias (vs High risk)	23, 1798		*0.044*	47.2%, p = 0.009	23, 1798		*<0.001*	13.7%, p = 0.284
Some concerns		-0.34 (-0.65, -0.04)	0.028			-0.21 (-0.48, 0.06)	0.134	
Low risk		-0.11 (-0.39, 0.16)	0.419			-0.05 (-0.29, 0.19)	0.689	
Triglycerides, mM	**23, 1742**			**49.0%, p=0.005**	**23, 1742**			**49.0%, p=0.005**
Mean baseline age, per 10 y	23, 1742	-0.05 (-0.11, 0.02)	0.149	51.3%, p = 0.003		-	-	-
Mean baseline BMI, kg/m^2	23, 1742	0.00 (-0.02, 0.02)	0.962	50.3%, p = 0.004	23, 1742	0.01 (-0.02, 0.03)	0.667	52.4%, p = 0.003
Mean baseline level	22, 1721	-0.20 (-0.63, 0.22)	0.350	45.1%, p = 0.014	22, 1721	-0.13 (-0.53, 0.26)	0.508	31.7%, p = 0.087
Sedentary effectiveness, h/day [c]	22, 1721	-0.06 (-0.17, 0.05)	0.279	45.9%, p = 0.012	22, 1721	-0.13 (-0.21, -0.05)	0.001	0.0%, p = 0.507
Duration (vs ≤3 months)	23, 1742		*0.645*	53.4%, p = 0.002	23, 1742		*0.447*	55.7%, p = 0.001

3–6 months		-0.07 (-0.24, 0.10)	0.402			-0.05 (-0.24, 0.14)	0.639	
>6 months		-0.06 (-0.25, 0.13)	0.516			-0.07 (-0.28, 0.13)	0.481	
Risk of bias (vs High risk)	23, 1742		*0.396*	53.6%, p = 0.002	23, 1742		*0.485*	55.7%, p = 0.001
Some concerns		-0.13 (-0.33, 0.07)	0.218			-0.07 (-0.34, 0.19)	0.587	
Low risk		-0.10 (-0.28, 0.07)	0.245			-0.06 (-0.28, 0.16)	0.573	

Table presents unstandardized regression coefficient (*b*) and 95% confidence interval (CI) and *p* value from meta-regression of controlled trials of adult sedentary behaviour interventions ≥7 days. Italics indicates overall p value (omnibus test).

[a] k = total number of interventions included and n = total number of individuals analysed in the included interventions, in the meta-regressions or main meta-analysis (boldface) [b] Residual heterogeneity (I^2 and p from Cochrane's Q test) with overall heterogeneity in the main meta-analysis shown in boldface [c] Estimated effectiveness of intervention on overall sedentary time (net of control) [d] No studies in the 3–6 month duration category.

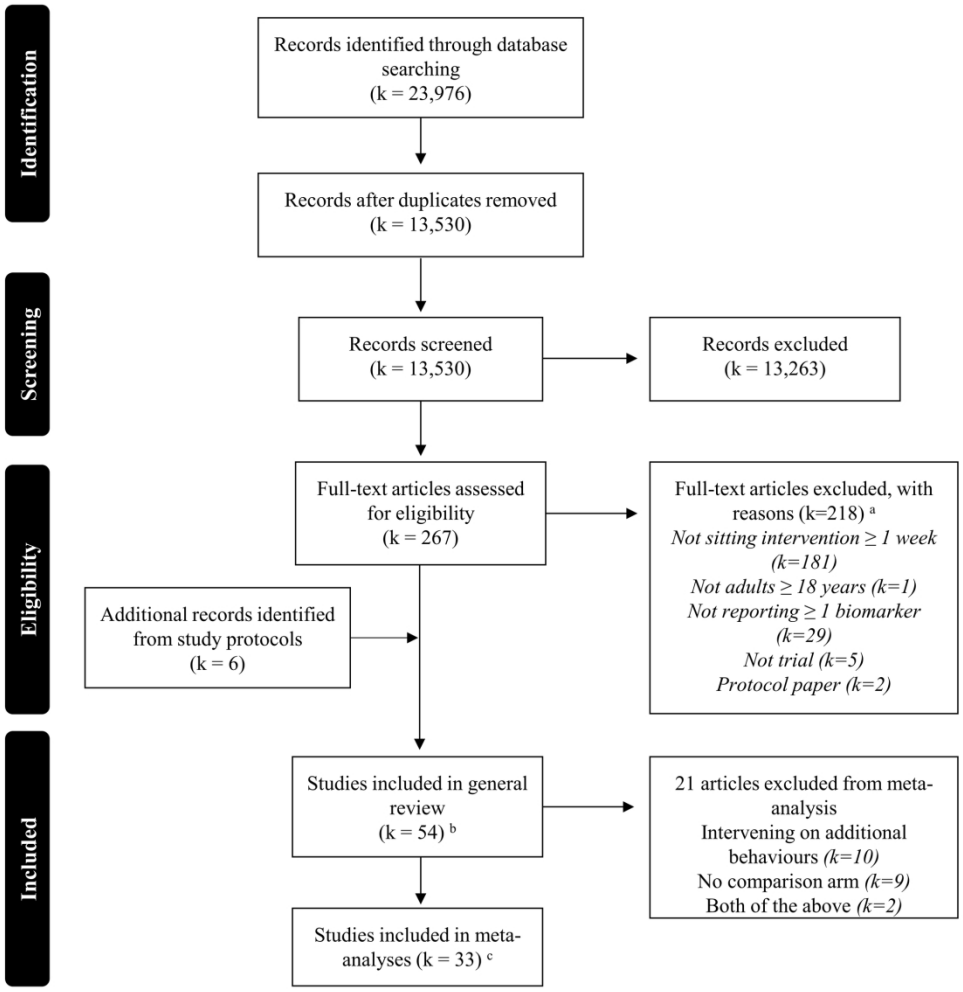


Fig. 1 PRISMA diagram of the literature search results.

190x190mm (300 x 300 DPI)

Supplemental Material S1 Searches performed for Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R)

#	Searches	Results[a]
1	Sedentary Lifestyle/ or Television/ or Computers/ or Video Games/	0
2	(sitting or sedentary).tw.	5374
3	((reclining or lying) adj4 (time* or bout* or posture* or position*1)).tw.	264
4	((screen or screens or screenbased or TV or television* or computer* or device* or smartphone* or phone* or tablet* or ipad* or DVD or video*) adj4 (time* or hours or watch* or view*)).tw.	4377
5	((computer* or internet*) adj ("use" or "useage" or "usage" or behavio?r*)).tw.	543
6	((reading or gaming) adj3 time*).tw.	276
7	((videogam* or video game* or computer game* or electronic game*) adj5 (time* or bout* or hours or watch* or view*)).tw.	103
8	Automobile Driving/	0
9	((car or cars or automobile* or driving or commute* or commuting) adj3 time*).tw.	254
10	(physical* adj3 inactiv*).tw.	1158
11	((inactive or inactivity) adj3 (time* or bout* or hours)).tw.	102
12	(low adj2 energy expenditure*).tw.	34
13	(low adj2 physical activity*).tw.	357
14	or/1-13	11977
15	((cardiovascular or cardiometabolic or cardio-metabolic) adj2 risk*).tw.	10453
16	(metaboli* or dysmetaboli*).tw.	92550
17	body mass index/ or exp overweight/ or waist circumference/ or waist-hip ratio/	0
18	Body Weight/ or Weight Loss/ or Weight Gain/ or exp Adipose Tissue/ or Adiposity/ or body composition/ or body fat distribution/	0
19	exp Blood Pressure/ or exp Proinsulin/ or exp Adipokines/ or exp Somatomedins/ or exp Lipids/	0
20	Hemoglobin A, Glycosylated/ or Biological Markers/	0
21	C-Reactive Protein/ or Tumor Necrosis Factor-alpha/ or Interleukin-6/ or exp Fibrinogen/	0
22	(glycosuria* or hyperglyc?emi* or hyperinsulin* or hypertensi* or prehypertensi*).tw.	37777
23	(glucose or blood sugar* or glyco* or glyca* or glyce*).tw.	79568
24	(overweight or over-weight or obesity or obese or BMI or body mass index or body mass indicator*).tw.	49646
25	(waist circumference* or waist-hip ratio* or adiposity or adipose or fatty tissue*).tw.	13449
26	(weight adj1 (gain* or increase* or loss* or decrease* or reduc* or lose* or losing or fluctuat*)).tw.	16489
27	(body adj (fat or composition or weight)).tw.	20018
28	(blood pressure or diastolic or systolic).tw.	27762
29	(proinsulin* or insulin* or c-peptide* or adiponectin* or leptin* or resistin* or somatomedin*).tw.	28561
30	(lipid* or triglycerid* or triacylglycerol* or lipoprotein* or apolipoprotein* or apoprotein* or chylomicron* or diglycerid* or diacylglycerol*).tw.	49109
31	(dyslipid* or dyslipoprotein* or hyperlipid* or hyperlip?emi* or lip?emi* or lipid?emi* or hypercholesterol* or hyperlipoprotein* or hypertryglycerid*).tw.	8511
32	(HDL or LDL or VLDL or cholesterol*).tw.	19137

33	(biologic* marker* or biomarker* or immun* marker* or biochemical marker*).tw.	34917
34	(c-reactive or crp or fibrin* or hscrp or homocystein*).tw.	14516
35	(il6 or il-6 or interleukin-6 or tumo?r necrosis factor alpha or tnf-a or tnf-alpha).tw.	19760
36	((glycate* or glycosylate*) adj2 (hemoglobin* or haemoglobin*)).tw.	2598
37	(hb a1* or hba1*).tw.	4575
38	(HOMA or homeosta* model assessment*).tw.	2421
39	or/15-38	334401
40	movement/ or locomotion/ or walking/ or motor activity/ or exercise/ or resistance training/	0
41	physical exertion/ or physical fitness/	0
42	accelerometry/ or actigraphy/	0
43	(acceleromet* or accelero-met* or pedomet* or inclinomet* or actigraph* or acti-graph* or actimet* or acti-met*).tw.	3271
44	((activit* or movement* or motion or fitness) adj2 (monitor* or assess* or measure* or track* or sensor*)).tw.	10370
45	(physical* adj2 (fit* or activ* or train*)).tw.	14689
46	(ambulation* or ambulatory activit* or walk or walking).tw.	12556
47	((light or moderate or intensity) adj2 activit*).tw.	2040
48	(step or steps or stepping).tw.	76852
49	(sit-stand* or stand-step* or standing).tw.	10846
50	(GT1M or GT3X or GT3X+ or activPAL or Fitbit or GENEactiv or Jawbone or LUMOback or Fuelband or Omron).tw.	413
51	(Actiheart or Actical or Movemonitor or Tractivity or Yamax or Sensewear or Misfit or IDEEA or DirectLife or SmartShoe).tw.	700
52	(3dNX or ADXL322 or DynaPort MiniMod or EGAS device or GENEA or Minimod or RT3 device).tw.	9
53	(Digi-Walker or Caltrac or RT3 triaxial or Tracmor2 or Lifecorder or Walk4Life).tw.	13
54	(StepWatch or TriTrac or Axivity or BioTrainer or Activ Tracer or ActiWatch or ActivTracer or Mini-Motionlogger).tw.	54
55	or/40-54	122156
56	(randomized controlled trial or controlled clinical trial).pt.	307
57	(random* or quasirandom* or trial or placebo).tw. or clinical trial*.sh.	156307
58	cross-over studies/ or (cross-over or crossover).tw.	9949
59	or/56-58	162180
60	14 and 39 and 55 and 59	402
61	exp animals/ not humans.sh.	1
62	60 not 61	402
63	limit 62 to english language	399

[a]Results are displayed for the initial search (March 03 2017). Identical searches were performed, ultimately covering research up to February 16 2018.

Supplemental Material S2 Rules used for extracting data for the meta-analyses

Consideration	Rule [a]
Quality control	One enters, another checks, discrepancies are discussed and resolved.
Intervention selection	The sedentary-behaviour only intervention in a factorial design. All sedentary behaviour interventions within a study for multiple differing interventions. *NOTE: The only meta-analysed multi-arm studies were Taylor et al. 20xx (both included) and Kozey-Keadle et al. 2014 (only one intervention included).*
Endpoint selection	End of intervention. If unavailable, use interim results or results averaged across several follow-up endpoints (only if the authors indicate no difference between these follow-up endpoints.) *NOTE: all estimates extracted were end of intervention except Balducci 2017 reported some outcomes not in Balducci 2019.*
Statistical conversions	$SE =$ (Upper – Lower Limit)$/(2 \times 1.96)$ and $SE = SD/\sqrt{n}$.
Unit conversions*	1 kg = 0.453592 pounds 1 inch = 2.54 cm 1 mM = 18 mg/dl (glucose) 1 mM = 38.67 mg/dl (cholesterol) 1 mM = 88.57 mg/dl (triglycerides) 1 µU/mL = 6 pmol/L insulin NGSP HbA1c = (0.09148*IFCC HbA1c) + 2.152 eAG = 1.59 * NGSP HbA1c - 2.59 Percentage of baseline values: * baseline values / 100
Intervention effect extraction (minimum required data = intervention effect and its SE)	To maximise the amount of available data while retaining sufficient similarity for pooling. In order of preference extract: *Intervention effects (between-group differences in change, in units)* 1. As reported 2. Calculated from each group's reported mean changes 3. Calculated from each group's reported means at baseline and follow-up (i.e., follow-up mean – baseline mean). 4. By requesting sufficient data to apply #1 or #2 from the authors *Standard Error (SE) of intervention effect above* 1. From reported SE or 95% Confidence Intervals (CI) 2. By performing an independent samples t-test from within-group data, using standard deviations (SD) or SE of change 3. By requesting sufficient data to apply #1 or #2 from the authors 4. By performing an independent samples t-test of using (SD) within-group data, using standard deviations (SD) or SE at end of intervention. *NOTE: Data were requested from 11 authors and 5 provided data while 6 did not respond or could not acquire the data, leading to the use of estimates from end-of-intervention SE for 4 studies and data being unreportable from 2 studies.*

Outcomes in review but not in paper	This is a high-burden request. Contact authors and request only when a very similar outcomes was reported (e.g., fat mass / percentage body fat, weight / BMI, cholesterol ratios / values) and request only from authors on the research team. *NOTE: This occurred for Alkahjah et al 2019, Healy 2013 and Healy 2017.*
Errors suspected	In order of preference 1. attempt to verify mathematically and resolve mathematically from other data reported 2. contact authors *NOTE: Authors contacted were Ashe et al (2015) (large weight discrepancy; verified outcomes were correct); Biddle et al. (2015) (identical values for >1 outcome; provided new data); Mantzari et al (2019) (95% CI not logical; provided new data); Thomsen et al. 2016 and Thomsen et al. 2017 (impossible units mM HbA1c; responded was eAG mM, with the following conversion formula listed in unit conversions)*

[a] The same general procedures were applied in extracting intervention effects on sedentary behaviour outcomes, and baseline values of age and the biomarker outcomes, except that authors were not contacted to obtain further baseline data, only intervention effects.

Table S3: Study and intervention characteristics

Study Details			Intervention details					
Study (Year); Country	**Population**	**Design***	**Duration**	**ME**	**Intervention Delivery (setting)****	**Sedentary target/messaging**	**Other behaviours**	**Primary outcome(s)**
Aadahl et al. (2014); Denmark	95F, 71M $\bar{x}$=52.0 years (18-69) $\bar{x}$=27.3 kg/m^2 (all) Ethnicity not reported Sedentary & Inactive	RCT	6 months	×	**I: C/ED (community)** -*C/ED* (4x FtF sessions, each 6 weeks, 30-45 min, nurse delivered) **C:** Usual conditions	1) Reduce TV 2) Swap sitting with standing 3) break up prolonged sitting via standing 4) All sitting bouts ≤ 30 min	Standing	Sitting time (all)
Alkhajah et al. (2012); Australia	29F, 3M $\bar{x}$=36.3 years (20-65) $\bar{x}$=22.1kg/m^2 (all) 88% C/W FT workers (office)	nRCT	3 months	×	**I: Environmental (workplace)** -*EM* (individual sit-stand workstation) -*EM-ED* (1x Ftf demonstration [≈2 min] + written instructions on use) **C:** Usual conditions	Reduce sitting	Standing	Sitting time (work)
Alonso-Dominguez et al. (2019); Spain	93F, 111M $\bar{x}$= 60.6 years (25-70) $\bar{x}$= 29.9 kg/m^2 (all) Ethnicity not reported Type 2 diabetes	RCT	3 months	9M	**I: Multicomponent (primary healthcare)** - *C/ED* (10 min FtF information provision diet/PA; 1 h FtF workshop on use of app) - Structured exercise (5x FtF moderate intensity 4 km walks (1/week for 5 weeks), nurse-delivered) - *Device self-monitoring* (app; removed at 3 months) **C:** Usual care: (+ 10 min FtF information provision on diet / PA)	Reduce sedentary time	1) Diet 2) PA (steps, MVPA)	PA (steps)

Ashe et al. (2015); Canada	25F, 0M (women) $\bar{x}$=64.1 years (55-70) $\bar{x}$=29.3 kg/m^2 (all) Ethnicity not reported Inactive	RCT	6 months	×	**I: Multicomponent (community)** -*C/ED* (9x FtF sessions: ≈1h group & ≈10-15 min individual PA prescription delivered by exercise physiologist; + ≈1h group brainstorming delivered by project staff) - *Device self-monitoring* (Fitbit) **C:** Attention control (Non-activity health information)	Reduce sitting time	1) PA (total) 2) Various (e.g., diet, bone health, public transport)	Feasibility
Balducci et al. (2019); Italy	116F, 184M $\bar{x}$= 61.7 years (40-80) $\bar{x}$=30.1kg/m^2 (27-40) Ethnicity not reported Type 2 diabetes Sedentary & Inactive	RCT	36 months	×	**I: Multicomponent (primary care)** -*C/ED* (1x FtF session, 30 min, diabetologist-delivered) -*Structured exercise* (8x FtF sessions 30 min aerobic, 30 min resistance, 15 min warm up/cool down incl. stretching, 'exercise specialist' delivered). **C**: Usual care	PA instead of sitting time in all settings	PA (LPA, MVPA, resistance)	1) Sitting time (all) 2) PA
Ball et al. (2017); Australia	46F, 36M $\bar{x}$= ? years (40-65) $\bar{x}$=30.6kg/m^2 (all) Ethnicity not reported Sedentary & Inactive	PP	4 months	×	**I: Multicomponent (community)** - *C/ED* (1 x Tel session, research staff delivered, 20 min) -SMS goals, prompts (≈16 at 1/week) -*Financial incentives* (dependent on goal attainment) -*Device self-monitoring* (Fitbit)	Reduce sitting time (particularly during leisure but also at work)	PA (total)	PA
Bergman et al. (2018); Sweden	44F, 36M $\bar{x}$= 51.4 years (40-67) $\bar{x}$= ? kg/m^2 (25-40) Ethnicity not reported Workers (office, have sit-stand desk, sedentary work tasks) Inactive (limited aerobic training)	RCT	13 months	×	**I_1: Multicomponent (workplace)** - *EM:* Treadmill workstation - *C/ED*: (1x FtF nurse-delivered health consultation including SB, diet and PA), 4x emails (sedentary behaviour & treadmill use) **C:** Usual care (+1x FtF nurse-delivered health consultation PA, diet)	Reduce sedentary time using treadmill (self-selected walking speed, ≥1 h/day)	1) PA (walking) 2) Diet	PA (weekday & weekend walking, activPAL)

Biddle et al. (2015); UK	128F, 59M $\bar{x}$=32.8 years (18-40) $\bar{x}$=34.6 kg/m^2 (≥25)*** 80% C/W At risk for type 2 diabetes or obese***	RCT	12 months	✕	**I: Multicomponent (community)** - *C/ED* (1x FtF group structured education workshop, 3h +1x Tel call, [duration unknown]) -*Device self-monitoring* (Gruve) **C:** Attention control (information leaflet on diabetes, PA and sedentary)	Reduce sedentary behaviour	Standing	Sitting time (all)
Butler et al. (2018); USA	8F, 13M $\bar{x}$= 22.7 years (≥18) $\bar{x}$= 23.0 kg/m^2 (all) 71.4% C/W / 23.8% Black / 4.8% Hispanic University students ≥5 h/week in a specific building	RCT-x	3 weeks	✕	**I: Environmental (university)** -*EM*: Shared standing desks (classroom) **C**: Usual conditions	Replace classroom sitting with standing, ≈5 h /week	Standing	Cardiometabolic biomarkers
Carr et al. (2013); USA	36F, 4M $\bar{x}$=44.7 years (adults) $\bar{x}$=32.4 kg/m^2 (≥25) 70% C/W FT workers (desk) Inactive	RCT	12 weeks	✕	**I: Multicomponent (workplace)** -*C/ED* (website messaging: motivational including prompting, 1 message /day + 3 emails/week, ≈120 total) -*EM* (individual portable pedal machine with PC software) -*EM-ED* (researcher-assisted setup & instruction on use + website prompts for usage) - *Device self-monitoring & social comparison* (pedometer challenge) **C:** Usual conditions (waitlisted for I)	Reduce sedentary time	1) Standing 2) PA (steps, pedalling)	1) Sitting time (all) 2) PA

Danquah et al. (2017); Denmark & Greenland	210F, 107 M $\bar{x}$=46 years (19-64) $\bar{x}$=26 kg/m^2 (all) Ethnicity not reported FT workers (office)	c-RCT	3 months	×	**I: Multicomponent (workplace)** -*EM* (general walking routes + shared high tables) -*C/ED* (FtF 1x 15 min lecture & workshop [duration unknown]) -*Online/SMS support* (weekly emails or 2/week SMS, ≈12-24 total) **C:** Usual conditions	Reduce sitting time	1) Standing 2) PA (steps)	Sitting: time, prolonged time, accumulation (work)
Dunning et al. (2018); South Africa	12F, 8M $\bar{x}$= 27.5 years (18-45) $\bar{x}$= 23.8 kg/m^2 (≤30) Ethnicity not reported Workers (desk, sedentary at work)	RCT	10 weeks	×	**I: Environmental (workplace)** *SMS prompts / reminders:* (every 30 min during work hours) **C**: Usual conditions	Break up prolonged sitting	Short bouts LPA (standing or ambulatory)	Sedentary or sitting time (activPAL and actiGraph <100 counts/min)
Eakin et al. (2014); Australia	132F, 170M $\bar{x}$=58.0 years (20-75) $\bar{x}$=33.1 kg/m^2 (25-45) 87% C/W Type 2 diabetes Inactive	RCT	18 months	6M	**I: C/ED (community)** -*C/ED only* (4x weekly + 5x fortnighly + 12x monthly calls, 20-30 min) **C:** Usual care	1) Sit less 2) Break every 30 min 3) ≤2 h non-work screen time	1) Diet 2) Weight loss 3) PA (MVPA, resistance)	1) PA 2) Weight 3) HbA1c
Garland et al. (2018); USA	27F, 40M <40 years (63%) $\bar{x}$= 24.8 kg/m^2 (all) Ethnicity not reported Workers (office)	c-RCT	12 months	×	**I: Multicomponent (workplace)** -EM (individual sit-stand workstation) - *C/ED* (1x FtF group structued education session + ergonomic education on workstation) **C:** Usual care (same group session as I, information only)	Reduce prolonged sitting	Increase movement	None stated

Gill et al. (2019); Canada	93F, 25M $\bar{x}$= 57.7 years (18-85)* $\bar{x}$≈ 31.4 kg/m^2 (>25*) 98% C/W At risk for CVD (1+ out of: >25 kg/m2, sedentary ≥3h/d, inactive <150 min/wk MVPA, < 8 fruit & veg serves/day, type 2 diabetes)	RCT	6 months	6M (app & Online tools only)	**I: C/ED (community)** -*C/ED* (Online & app supported health coaching with exercise prescription & SB advice (4x FtF sessions [≈30-40 min] at 0, 2, 4, 6 months), telephone coaching, app-based virtual coaching) -*Device, app & web-based self-monitoring, networking/support & social comparison* **C:** Usual conditions (waitlisted for I until 6 months)	Reduce sedentary time	1) PA (steps, MVPA) 2) Diet	PA (step count)
Graves et al. (2015); UK	37F, 10M $\bar{x}$=38.6 years (≥18) $\bar{x}$=24.8 kg/m^2 (all) 96% C/W FT workers (office)	RCT	8 weeks	×	**I: Environmental (workplace)** -*EM* (individual sit-stand workstation) -*EM-ED* (Manufatcturer brief FtF demonstration + web information, ergonomics only) **C:** Usual conditions	Reduce workplace sitting	Standing	Sitting time (work)
Harris et al. (2017); UK	32F, 18M $\bar{x}$=42.0 years (≥18) $\bar{x}$=40.7 kg/m^2 (≥30) 96% C/W Intellectual disabilities	c-RT	12 months	×	**I_1: Multicomponent (community)** -*C/ED* (9-12x initial + 6x maintenance FtF sessions with participant & carer, 40-60 min, delivered by dietician & health professional) -*Device self-monitoring* (pedometer) **I_2: Alternate Intervention: W**eight loss heath education ("Weight Watchers Too")	Reduce sedentary behaviour	1) Diet 2) Weight loss 3) PA (LPA, MVPA)	Weight

Healy et al. (2013); Australia	24F, 19M $\bar{x}$=43.2 years (18-65) $\bar{x}$=26.8 kg/m^2 (all) 88% C/W FT workers (office)	nRCT	4 weeks	×	**I: Multicomponent (workplace)** -*C/ED* (1x FtF session 30 min including EM setup & demonstration & 3x Tel calls, weekly 7-10 min) -*Device feedback* (1x, activPAL, accelerometer) -*EM* (individual sit-stand workstation) -*Organisational* (emails, 1x educational workshop generating strategies) **C:** Usual conditions	1) Stand Up every ≤30 min 2) Sit Less via workstation, gradually aiming ≈ 50/50 sitting with frequent postural change 3) Move More via incidental PA	1) Standing 2) PA (incidental PA, predominantly LPA)	Sitting time (work)
Healy et al. (2017); Australia	158 F, 73 M $\bar{x}$=45.6 years (18-65) $\bar{x}$=28.6 kg/m^2 (all) 80% C/W FT workers (office)	c-RCT	12 months	9M non-contact (EM only)	**I: Multicomponent (workplace)** -*C/ED* (1xFtF session 30 min including EM setup & demonstration + 4x Tel health coaching calls, 7-10 min, tapered: first 3M) -*Organisational support* (1x workshop generating strategies + 6x workplace-delivered emails: first 3M) -Device feedback (1x, activPAL, accelerometer) -*EM* (individual sit-stand workstation) **C:** Usual conditions	At work & elsewhere to: reduce sitting and reduce prolonged sitting in ≥30 min bouts. Target: Gradually aiming ≈50/50 sitting / not	1) Standing 2) PA (LPA primarily)	Sitting time (work)
Igelstrom et al. (2014); Sweden	24F, 86M $\bar{x}$=55 years (adults) $\bar{x}$=34.4 kg/m^2 (≥25) Ethnicity not reported Obstructive sleep apnoea	RCT	18 months	×	**I: C/ED only (hospital)** -*C/ED* (14 FtF sessions [duration unknown], tapered, covering PA, diet & CPAP use - dietician & physiotherapist delivered) **C:** Usual care (CPAP instruction)	Reduce sedentary time	1) Diet 2) PA (LPA, MVPA) 3) CPAP use	1) PA (MVPA) 2) Diet

John et al. (2011); USA	7 F, 5M $\bar{x}$=46.2 years (20-65) $\bar{x}$=33.9 kg/m^2 (>28) Ethnicity not reported Workers (office)	PP	9 months	×	**I: Environmental (workplace)** -*EM* (individual treadmill desk)	Replace desk-sitting with treadmill stepping (self-directed amount & speed)	PA (stepping)	None stated
Kallings et al. (2009); Sweden	58 F, 43 M $\bar{x}$≈68 years (67-68) $\bar{x}$=30.1kg/m^2 (25-40) Ethnicity not reported Inactive	RCT	6 months	×	**I: Multicomponent (primary care)** -*C/ED* (1x 30-min FtF session PAP & Counselling, lecture, Tel follow-up - health-professional delivered) - *Device self-monitoring* (pedometer) **C:** Usual care (+written materials about health & PA)	Reduce sedentary time	PA (MVPA, resistance, flexibility/ balance)	PA
Koepp et al. (2013); USA	25F, 11M $\bar{x}$=42 years (adults) $\bar{x}$=29 kg/m^2 (all) Ethnicity not reported Workers (desk)	PP	12 months	×	**I: Environmental (workplace)** -*EM* (individual treadmill desk)	Replace desk-sitting with treadmill stepping (self-directed)	PA (stepping)	PA
Kozey Keadle et al. (2014); USA	39F, 19 M $\bar{x}$=43.6 years (20-60) $\bar{x}$=35.1 kg/m^2 (all) Ethnicity not reported Workers (sedentary at work) Inactive	≈RCT & ≈RCT-x (4 arm)	12 weeks	×	**I_1: Multicomponent (community)** - *C/ED* (12x FtF sessions, [duration unknown], covering sedentary behaviour & non-exercise activity. Told not to exercise.) - *Device self-monitoring* (pedometer) **I_{2-3}:Alternate interventions:** exercise, exercise & sedentary behaviour **C:** Usual behaviour	Decrease sedentary time (home & work) by increasing non-exercise activity and do not exercise [I_1].	PA (LPA, steps)	Cardio-respiratory fitness

Lai et al. (2019); China	37F, 19M $\bar{x}$=? years (≥18) $\bar{x}$=? kg/m^2 (all) ?% Chinese Workers	PP	3 months	×	**I: C/ED only (workplace)** - *C/ED* (1 x 3 h FtF session initially, 1 x 1 h FtF session at 1 month) - *Structured exercise* (unsupervised, demonstration only as part of *C/ED*)	Reduce sedentary behaviour	1) PA (Zero-time strength and stamina exercises)	1) PA (engagement with zero-time strength and stamina exercises)
Lin et al. (2017); Taiwan	52F, 47M $\bar{x}$=49.5 years (≥20) $\bar{x}$=24.0 kg/m^2 (all) Ethnicity not reported FT workers (sedentary job)	c-nRCT	12 weeks	×	**I: Multicomponent (workplace)** - *C/ED* (3x newsletters; handbook w/ goal setting & relapse prevention) - *Device self-monitoring & social comparison* (team pedometer challenge each 2 weeks) -*Computer prompt* (break hourly) -*EM* (walking routes, maps, signage, prompts) **C**: Usual conditions (+newsletter)	Sit less, walk more	PA (steps)	1) Sitting time (work, all) 2) PA 3) Cardio-metabolic biomarkers 4) Work productivity
Lyons et al. (2017); USA	34F, 6M $\bar{x}$=61.5 years (55-79) $\bar{x}$=30.3 kg/m^2 (25-35) 65% C/W, 13% Black, 15% Other, 28% Hispanic Inactive	RCT	12 weeks	×	**I: Multicomponent (community)** - *C/ED* (12x Tel calls, weekly, 15-20min, behavioural counsellor) -*Device self-monitoring & social comparison* (Jawbone Up/app) **C**: Usual conditions	Reduce prolonged sedentary bouts (bout goal 1 h suggested, negotiated)	PA (steps)	Feasibility
MacEwen et al. (2017); Canada	23F, 5M $\bar{x}$= 45.5 years (18+) $\bar{x}$= 35.8 kg/m^2 (WC >= central obesity) Ethnicity not reported FT worker (desk)	RCT	12 weeks	×	**I: Environmental (workplace)** -*EM* (individual sit-stand workstation) -*EM-ED* (instructed to sit or stand as desired and exercise as normal) **C:** Usual conditions	No messaging: sit or stand as much as desired	Standing	Not stated
Mailey et al. (2016); USA	49F, 0M (women) $\bar{x}$=38.7 years (≥21) $\bar{x}$=? kg/m^2 (all) 84% C/W FT workers (sedentary job) Inactive	RT	8 weeks	×	**I: C/ED (workplace)** -*C/ED* (1x FtF session covering strategies, 1x Tel follow-up, self-monitoring)	Decrease sedentary time by 30 min workday with breaks of 1-2 min each half hour (short breaks) or 2x 15 min breaks	PA (LPA, MVPA)	Sitting time (work)

Mainsbridge et al. (2014); Australia	24F, 5M $\bar{x}$=40.2 years (adults) $\bar{x}$=? kg/m^2 (all) Ethnicity not reported FT workers (desk)	RCT	13 weeks	×	**I: Environmental (workplace)** - *Computer prompts only* (interactive computer software) **C:** Usual conditions (+ 1x information session)	Break up prolonged sitting every 45 min with short bursts of NEPA	PA (non-exercise PA, especially LPA)	Mean arterial pressure
Malaeb et al. (2019); USA	23F, 2M $\bar{x}$=47.7 years (>18) $\bar{x}$=28.5 kg/m^2 (all) Ethnicity not reported Workers (Sedentary job 'mostly sitting')	RCT-x	2 weeks	×	**I: Environmental (workplace)** -*EM* (shared treadmill desks) -*EM-ED* (demonstration, leaflet, self-monitoring, adherence checks) **C:** Usual conditions	Reduce sitting by using treadmill desk 2.5 h/d, 5 d/week	1) PA (walking; Non Exercise Activity Thermogenesis)	Not stated
Mantzari et al. (2018); UK	≈ 11 F, 9M (n=18, 61% F) $\bar{x}$=43.4 years (adult) $\bar{x}$=25.1 kg/m^2 (all) Ethnicity not reported ≥0.6 FT workers (office, doing ≥70% work at same desk)	RCT	3 months	×	**I: Multicomponent (workplace)** -*EM* (individual sit-stand workstation) -*EM-ED* (demonstration by research staff + instructional leaflet, self-monitoring use by diary) **C:** Usual conditions (+ brief information prolonged sitting)	Break up prolonged sitting time	1) Standing	Feasibility
Maxwell-Smith et al. (2019); Australia	34F, 34M $\bar{x}$=64.1 years (18-80) $\bar{x}$=28.3 kg/m^2 (all) 97.1% C/W Stage 1-2 colorectal or endometrial cancer survivors completed active treatment last 5 y, at CVD risk Inactive (<150 min/wk MVPA)	RCT	12 weeks	×	**I: Multicomponent (community)** - *C/ED* (2x 2-hour Ftf group sessions at wk 1 and 4, delivered by health psychologists specialising in behaviour change for device setup, PA messaging, goal setting/planning, self-monitoring, exercise coaching, 1 x 20-min Tel call at week 8) - *Device self-monitoring & Prompts* (Fitbit Alta) **C**: Usual conditions (+ brief written materials on PA guidelines, example exercises)	Reduce bouts of sedentary behaviour	1) PA (steps, MVPA) 2) Strength exercises (home based)	PA (MVPA)

Maylor et al. (2018); UK	51F, 38M $\bar{x}$=43.4 years (18-70) $\bar{x}$=25.9 kg/m^2 (all) 83.3% C/W, 16.7% black & minority Workers (office, same desk ≥3 d/wk, sedentary at work)	c-RCT	8 weeks	×	**I: Multicomponent (workplace)** -*C/ED* (1x group FtF initial, 1 x individual FtF (20 min)), weekly Tel calls (5-10 min) by research staff) -*Device self-monitoring & social comparison* (pedometer step challenge) -*Device prompts* (self-selected computer software or app) -*Financial incentives* (shopping vouchers) -*EM* (signage prompts about sitting and PA, self-selected strategies: moving equipment further, reallocating space for non-desk work) **C:** Usual conditions	Reduce sedentary behaviour at work	1) PA (especially ambulation)	Workplace sitting (activPAL)
Miyamoto et al. (2017); Japan	6F, 25M $\bar{x}$= 61.8 years (adults) $\bar{x}$= 24.8 kg/m^2 (all) Ethnicity not reported Type 2 diabetes	RCT	12 weeks	×	**I_1: Multicomponent (hospital)** -*C/ED* (3x sessions, likely FtF, [duration unknown]: advice by physical therapist to increase non-locomotive PA) -*Device self-monitoring* (accelerometer) **I_2: Multicomponent (hospital)** -as per I_1 but targeting locomotive PA **C:** Usual Care (waitlisted for I)	Reduce sedentary time by increasing non-locomotive PA (I_1) or locomotive PA (I_2)	PA (non-locomotive PA [I_1] or locomotive PA [I_2])	1) Fasting glucose 2) HbA1c

Morgan et al. (2013); Australia	0F, 159M $\bar{x}$=47.5 years (18-65) $\bar{x}$=32.7 kg/m^2 (25-40) Ethnicity not reported	RCT (3 arm)	3 months	3M	**I_1 Multicomponent (community)** -*C/ED* (resource provision: 1x 25-min DVD, handbook, support book) -*Device self-monitoring* (pedometer) **I_2 Multicomponent (community)** -I_1 components -*C/ED* (website delivered education, 7x emails) -Website/app self-monitoring (CALORIEKING) **C:** Usual conditions	Reduce sitting time	1) Diet 2) PA (steps)	Weight
Overgaard et al. (2017); Denmark	29F, 14M $\bar{x}$= 45.8 years (20-65) $\bar{x}$= 32.9 kg/m^2 (>30 or WC > central obesity) Ethnicity not reported Inactive	RT	4 weeks	×	**I_1: C/ED (community)** - *C/ED* (1x FtF session [duration unknown]: advice to sit less) **I_2: Alternate Intervention (MVPA)**	Reduce sedentary behaviour	PA (non-sedentary [I1]; MVPA [I2])	1) Sitting time (all) 2) PA
Pesola et al. (2017); Finland	75F, 58M $\bar{x}$= 37.4 years (28-53) $\bar{x}$= 24.5 kg/m^2 (≤35) Ethnicity not reported Workers (sedentary at work, with kids 3-8y)	c-RCT	6 months	6M	**I: C/ED (community)** *C/ED* (1x 30 min lecture + 1x FtF session 30-60 min, 2x Tel calls, behavioural counsellor delivered) **C**: Usual conditions (+ delayed short version of the C/ED)	Reduce and break up sedentary time	PA (LPA)	Sitting: time, accumulation (all)
Peterman et al. (2019); USA	14F, 7M $\bar{x}$=34.8 years (18-55) $\bar{x}$=28.3 kg/m^2 (all) Ethnicity not reported FT workers (office, ≥ 6 h/d sedentary at work) Inactive (<5 h/wk MVPA)	RCT	4 weeks	×	**I: Environmental (workplace)** -*EM* (individual underdesk stationary cycle) -*EM-ED* (FtF: Initial advice on cycle use, self-monitoring + weekly adherence checks by research staff) **C:** Usual conditions	Reduce and break up sedentary behaviour at work, replacing 15 min / h with stationary cycling (≈2 h/d)	1) PA (stationary cycling)	1) VO2 max 2) 2-h postprandial glucose

Prince et al. (2018); Canada	15F, 23M $\bar{x}$=62.0 years (≥18) $\bar{x}$=29.7 kg/m^2 (all) Ethnicity not reported Coronary artery disease enrolled in cardiac rehabilitation	RT	8 weeks	×	**I_1: Multicomponent (hospital)** - *Device prompts* (VTAP thigh-worn monitor) - *Structured exercise (cardiac rehabilitation)* (2x FtF on-site 1-hour aerobic and strength exercise sessions, physiotherapist delivered). - *C/ED* (no sedentary component, but optional nutrition counseling, smoking cessation, diabetes and stress management, and psychosocial support) **I_2: Alternate intervention** (cardiac rehabilitation as per I without sedentary component)	Device prompts to break up prolonged sitting every 30 min with >2 min standing/movement during waking hours	1) PA (MVPA, resistance), 2) Diet	Recruitment, acceptability, completion, adherence rates
Puig-Ribera et al. (2015); Spain	171F, 93M $\bar{x}$=42 years (adults) $\bar{x}$=25.7 kg/m^2 (all) Ethnicity not reported Workers (office) Inactive	c-RCT	19 weeks	10 weeks	**I: Multicomponent (workplace)** - *C/ED* (website-delivered education +6 x emails, tapered) - *Social support* (blog) - *Device self-monitoring* (pedometer) **C:** Usual conditions	Decrease occupational sitting via incidental walking, then short walks, then long walks	PA (LPA, steps)	1) Sitting time (work) 2) PA (steps)
Reeves et al. (2017); Australia	90F, 0M (female) $\bar{x}$=55.3 years (18-75) $\bar{x}$=31.0 kg/m^2 (≥ 25) Ethnicity not reported Breast cancer	RCT	6 months	×	**I: Multicomponent (community)** - *C/ED* (16x 30 min Tel calls, tapered, delivered by dieticians trained in behavioural counselling) - *Device self-monitoring* (pedometer) **C:** Usual care	1) Reduce prolonged sedentary time 2) <2h/day non-work screen time	1) Diet 2) PA (MVPA)	Weight
Resendiz et al. (2019); USA	28F, 7M $\bar{x}$=? years (≥18) $\bar{x}$=32.2 kg/m^2 (≥25) Ethnicity not reported Workers (sedentary at work)	RCT	6 months	×	**I: Environmental modification (workplace)** *EM* (sit-stand workstation, with anti-fatigue mat, installed or checked by ergonomics staff) *ED-EM* (self-monitoring desk use and energy output, instruction on desk use)	Reduce sitting by use of desk, no target but starting at 10 min/h standing	1) Standing (desk)	None stated

Rosenberg et al. (2015); USA	17F, 8M $\bar{x}$=71.4 years (>60) $\bar{x}$=34.1 kg/m^2 (≥27) 91% C/W Sedentary	PP	8 weeks	×	**I: C/ED (community)** - *C/ED only* (5x Tel calls, 20-30 min, tapered delivered by 'health coach')	1) Reduce sitting time by 2 h/day via standing & moving 2) 15 more sit-stand transitions/day	1) Standing 2) PA (steps)	Sitting: time, accumulation (all)
Schuna et al. (2014); USA	40F, 1M $\bar{x}$=40.1 years (adults) $\bar{x}$=35.8 kg/m^2 (≥25) 20% C/W, 76% African American, 5% 'Other' Workers (desk, office)	RCT	3 months	×	**I: Multicomponent (workplace)** -*EM* (shared treadmill desks) -*EM-ED* (instruction on amout of use, online support: scheduled use with message reminders) **C:** Usual conditions	Reduce work sitting time via treadmill-desk use (2x/workday, 45 min/session).	PA (LPA, steps)	1) Sitting: time, accumulation (work) 2) PA (total)
Steeves et al. (2012); USA	46F, 12M $\bar{x}$=52.0 years (35-65) $\bar{x}$=33.5 kg/m^2 (25-45) 97% C/W, 3% African American Sedentary	RT	6 months	×	**I_1: Multicomponent (domestic)** -*C/ED* (3x monthly Ftf sessions, 3 x monthly Tel calls, newsletters) -*Device self-monitoring* (pedometer) **I_2:** Alternate intervention (Walking) -C/ED (3x monthly Ftf sessions, 3 x monthly Tel calls, newsletters)	Replace TV sitting with TV stepping at moderate pace (100-120 steps/min) during commercials of 30-90 min of TV ≥5x/week	PA (steps)	1) Feasibility 2) PA (total, steps) 3) Sitting (TV time; all)
Taylor et al. (2016); USA	152F, 33M $\bar{x}$=43.4 years (≥18) $\bar{x}$=30.3 kg/m^2 (all) 35% African American / 33% Non-Hispanic white / 32% Hispanic FT workers (sedentary worksites)	c-RCT (3 arm)	6 months	×	**I_1: Structured 'exercise' class (workplace)** -*Structured 'exercise'* at work (1x 15 min session/day, peer led) **I_2: Environmental (workplace)** - *Computer prompts* (3 min breaks 5x day) **C:** Usual conditions	Replace 15 min/day sitting with the breaks	PA (LPA, resistance, stretching)	None stated

Thomsen et al. (2016); Denmark	12F, 8M $\bar{x}$=59.3 years (≥18) $\bar{x}$=25.5 kg/m^2 (all) Ethnicity not reported Rheumatoid arthritis Sedentary & Inactive	RCT	16 weeks	×	**I_1: Multicomponent (hospital)** -*C/ED* (3x FtF sessions, 29-102 min, delivered by nurses trained in behavioural counselling) - *SMS prompts & goal reminders* (tailored, self-selected dose ≤5/week) **C:** Usual care	1) Swap sitting with standing at work & home 2) Reduce TV 3) Reduce prolonged sitting via standing 4) all sitting bouts <30 min	Standing	Feasibility
Thomsen et al. (2017); Denmark	121F, 29M $\bar{x}$= 59.6 years (adults) $\bar{x}$= 26.4 kg/m^2 (all) Ethnicity not reported Rheumatoid arthritis Sedentary & Inactive	RCT	16 weeks	×	**I: Multicomponent (hospital)** - *C/ED* (3x FtF sessions, 60-90 min, delivered by nurse/occupational therapist trained in behavioural counselling) - *SMS prompts & goal reminders* (tailored, self-selected dose) **C:** Usual care	1) Reduce TV 2) Swap sitting with standing 3) break up prolonged sitting via standing 4) All sitting bouts ≤ 30 min	Standing	Sitting time (all)
van der Pligt et al. (2018); Australia	160F, 0M (women) $\bar{x}$= 32.8 years (≥18) $\bar{x}$= 26.0 kg/m^2 (all) Ethnicity not reported Mothers	nRCT (3 arm)	9 months	×	**I_1: Multicomponent (community)** -*C/ED* (3x Tel calls, 30 min, dietitian delivered) -*Device self-monitoring* (pedometer & CALORIEKING site/app for diet) -*Online support* (behaviour therapy website for diet/PA & social support via discussion board) **I_2: Alternate intervention** -C/ED (child behaviour: separate study) **C:** Usual care (separate study)	Reduce sitting time at home and work	1) Diet 2) PA (incidental PA, planned walking, structured exercise)	1) Weight 2) Waist circumference

Verweij et al. (2012); Netherlands	194F, 329M $\bar{x}$=47 years (adults) $\bar{x}$=27.7 kg/m^2 (WC ≥overweight***) 89% Dutch nationality Workers Inactive***	c-RCT	6 months	×	**Multicomponent (workplace)** - *C/ED* (5x 20-30 min FtF counselling sessions, Occupational physician-delivered- choice of PA, diet or sedentary behaviour) -*Device self-monitoring* (pedometer) - *EM* (workplace audit / employer-negotiated change) **C:** Usual conditions (occupational physician delivered health risk assessment and advice)	Decrease sedentary behaviour (or work on one of the other behaviours)	1) Diet 2) PA (MVPA)	1) Waist circumference 2) PA (implied MPA, VPA) 3) Diet
Wyke et al. (2019); UK, the Netherlands, Norway, Portugal	0F, 1,113M (men) $\bar{x}$=45.8 years (30-65) $\bar{x}$=33.2kg/m^2 (≥27 kg/m2) 90% 'native' to study country	RCT	12 weeks	9M	**I: Multicomponent (community)** - *C/ED/Structured exercise:* 12x 90 min structured exercise session using behaviour change techniques, delivered by football coaches - *Device self-monitoring, social comparison, reminders*: (SitFIT device + social media support + game-based app) **C:** Usual conditions (waitlist for I)	Reduce sedentary time	1) PA (MVPA) 2) Diet	1) Sedentary time 2) PA
Yang et al. (2017); Taiwan	32F, 21M $\bar{x}$= 33.2 years (20-56) $\bar{x}$= 28.8 kg/m^2 (≥24***) Ethnicity not reported Metabolic abnormalities***	RCT-x	6 months (3 months I & 3 months C)	×	**I: Multicomponent (primary care)** - *C/ED* (12x 'Line' and email contacts, weekly, with health professional advice, information and reminders + website information) - *Device self-monitoring, social comparison, reminders* (sensor + smartphone app + website) **C**: Usual care (booklet with health information)	Sedentary time < 8h	1) Diet 2) Sleep 3) PA (total)	1) Sitting time (all) 2) PA

Zhu et al. (2018); USA	27F, 9M $\bar{x}$= 39.1 years (18-65) $\bar{x}$= 25.8 kg/m^2 (all) 75% C/W FT workers	nRCT	18M	14M non-contact (EM only)	**I: Multicomponent (workplace)** - *C/ED* (4 months: worksite staff-delivered emails, promotional flyers, e-newsletters) -EM (18 months: individual sit-stand workstation + shared treadmill desks) **C:** Usual conditions (+ e-newsletters on energy, ergonomics and mindfulness, delivered by worksite staff)	Reduce sedentary behaviour (use sit-stand workstation and treadmill workstation)	1) PA (via treadmill desk) 2) Standing (via workstation)	Workplace sitting

Footnotes: ME = maintenance evaluation; F = female; M = male; I = intervention; C = control; FT=full-time; PA = Physical activity; LPA = light PA; MVPA = moderate-vigorous PA; MPA = moderate PA; VPA = vigorous PA; C/W = Caucasian/White as reported by study (Caucasian, White, British White, non-Hispanic White) ; ?= Data unreported.

***Study designs**: c- = cluster, n = non, R = randomised, C = controlled, T = Trial, -x = crossover, PP = pre-post study (single arm).

****Intervention components:** C/ED = counselling/education; EM = environmental modification; FtF = face-to-face; Tel = Telephone SMS = short message system.

*****Criteria only required if other criteria are not met. Must be: overweight and at risk for type 2 diabetes and/or obese BMI (≥27.5 for South Asians otherwise ≥30 kg/m^2) (Biddle); inactive and/or BMI >=25 (Eakin); insufficiently inactive and/or >=overweight WC and/or not meeting diet recommendations (Verweij); above the threshold for BMI or one of the other 5 cardiometabolic biomarker risk factors (Yang).

Resendiz et al. (2019) average age is median

Supplementary Table S4 Baseline anthropometric characteristics (mean ± SD) and effects on sedentary behaviour in controlled trials of 34 adult sedentary behaviour interventions ≥7 days

Study	SB effectiveness [a]	Weight	BMI	Waist	Body fat	Fat mass	Fat-free mass	Systolic BP	Diastolic BP
	min/day	*kg*	*kg/m²*	*cm*	*%*	*kg*	*kg*	*mmHg*	*mmHg*
Aadahl et al. (2014)	-19.2	80.4 ± 16.3	27.3 ± 5.0	93.8 ± 13.5	32.5 ± 9.3				
Alkhajah et al. (2012)	-78.0	62.2 ± 9.4	22.1 ± 2.6	81.8 ± 8.8	29.2 ± 4.6	18.4 ± 4.5	44.1 ± 6.2		
Ashe et al. (2015)	-21.1	77.9 ± 19.2	29.3 ± 6.8					133 ± 15	82 ± 8
Balducci et al. (2019)	-48.0 [b]	84.1 ± 16.5	30.1 ± 5.1	103.6 ± 12.8	31.7 ± 10.2		56.5 ± 11.4	140 ± 20	83 ± 12
Biddle et al. (2015)	-7.2	98.6 ± 18.8	34.6 ± 5.1	103.3 ± 14.2	40.6 ± 7.1			120 ± 15	84 ± 10
Butler (2018)		70.6 ± 14.3	23.0 ± 3.0	74.4 ± 6.9					
Carr et al. (2013)	-18.2	89.4 ± 15.0	32.4 ± 4.7	92.7 ± 11.2				119 ± 13	76 ± 10
Danquah et al. (2017)	-27.0		26.0 ± 4.9	91.6 ± 13.0	30.2 ± 7.6	23.9 ± 11.1	53.4 ± 11.1		
Dunning et al. (2018)	-24.0	69.6 ± 9.9	23.8 ± 2.8		24.5 ± 7.9			109 ± 8	74 ± 8
Garland et al. (2018)	-41.1		24.8 ± 4.9						
Graves et al. (2015)	-51.6	68.8 ± 15.0	24.8 ± 4.5					119 ± 13	73 ± 9
Healy et al. (2013)	-82.6	80.2 ± 17.1	26.8 ± 5.4	91.2 ± 13.6	29.4 ± 10.0	24.2 ± 11.3	56.1 ± 11.3	131 ± 14	78 ± 8
Healy et al. (2017)	-36.3	80.2 ± 19.7	28.6 ± 6.1	93.6 ± 14.9	33.1 ± 9.5	27.0 ± 13.0	51.7 ± 11.1	127 ± 15	78 ± 11
Kallings et al. (2009)	-60.0	88.2 ± 12.6	30.1 ± 3.1	105.8 ± 8.5	36.7 ± 7.2	32.3 ± 7.5		140 ± 2	81 ± 1
Kozey-Keadle et al. (2014)	-88.3	99.4 ± 14.8	35.0 ± 4.7		45.5 ± 5.8			130 ± 10	79 ± 9
Lin et al. (2017)	-0.9	64.8 ± 12.1	24.0 ± 3.2	82.8 ± 9.4				118 ± 14	79 ± 10
Lyons et al. (2017)	-27.0	82.4 ± 10.9	30.3 ± 3.5		45.1 ± 5.3				
MacEwen et al. (2017)	-97.4	99.6 ± 24.6	35.8 ± 8.3	111.4 ± 13.6	42.7 ± 8.3			129 ± 12	86 ± 8
Mainsbridge et al. (2014)								135 ± 17	85 ± 14
Malaeb et al. (2019)		78.5 ± ?	28.4 ± ?		38.5 ± ?	28.5 ± ?	45.5 ± ?		
Mantzari et al. (2018)	-59.9	74.5 ± 14.7	25.1 ± 4.8	87.7 ± 13.5	26.8 ± 10.4			128 ± 13	78 ± 9
Maxwell-Smith et al. (2018)	8.6		28.3 ± 5.0					142 ± 18	86 ± 12
Maylor et al. (2018)	-1.0	76.4 ± 7.6	25.9 ± 0.5	86.5 ± 2.8	28.8 ± 1.4			126 ± 7	78 ± 5
Miyamoto et al. (2017)	-77.8	66.6 ± 3.9	24.6 ± 1.1						
Pesola et al. (2017)	11.3	71.9 ± 14.8	24.5 ± 3.8		27.8 ± 8.1			117 ± 11	74 ± 8
Peterman et al. (2019)	-12.1	79.0 ± 17.0	28.3 ± 6.7			28.5 ± 13.0	47.8 ± 8.1	112 ± 10	69 ± 8
Puig-Ribera et al. (2015)	-16.3		25.7 ± 4.4	87.9 ± ?				121 ± 17	78 ± 11

Resendiz et al. (2019)	-95.7		32.2 ± 5.2	96.8 ± 12.2					
Schuna et al. (2014)	-21.6	97.0 ± 24.5	35.9 ± 8.5		45.0 ± 5.6				
Taylor et al. (2016) – Booster breaks	-85.7	87.3 ± 15.1	31.2 ± 3.0	100.8 ± 8.3				117 ± 19	70 ± 8
Taylor et al. (2016) – Computer breaks	-87.7	78.6 ± 12.2	29.0 ± 2.6	96.5 ± 6.8				117 ± 17	70 ± 8
Thomsen et al. (2016)	-27.6	78.4 ± 17.3	25.5 ± 6.5	86.7 ± 18.5				128 ± 21	78 ± 11
Thomsen et al. (2017)	-132	75.2 ± 17.2	26.4 ± 5.4	92.1 ± 14.1				131 ± 20	78 ± 10
Zhu et al. (2018)	8.0	74.4 ± 18.1	25.8 ± 4.9					119 ± 15	76 ± 10

BMI = Body Mass Index; SB = Sedentary Behaviour; BP = Blood Pressure

[a] Effectiveness of intervention (net of control) in min / day on overall sedentary behaviour (SB) measured by self-report or device. When unreported, overall effects were loosely extrapolated from domain-specific effects (e.g., weekday and weekend reported separately) and exposure to the domain (e.g., 5 weekdays versus 2 weekend days/week). When only partial information was reported (e.g., workhours only) the extrapolation was based on the assumption of no effect outside of the reported domains. Percentages were converted to hours per day based on reported total amounts of time otherwise 8 hours working and 16 hours awake.

[a] For interim results reported in Balducci 2017, the corresponding value for effectiveness of intervention on sedentary behaviour is -33.0 min / day

Supplementary Table S5 Study baseline levels of blood biomarkers (mean ± SD) in controlled trials of 34 adult sedentary behaviour interventions ≥7 days

Study	TC	HDL	LDL	TG	Glucose	Insulin	HbA1c
	mM	*mM*	*mM*	*mM*	*mM*	*pmol/L*	*%*
Aadahl et al. (2014)	5.3 ± 1.0	1.5 ± 1.5	3.2 ± 3	1.2 ± 1.1	5.6 ± 1.0	52.1 ± 45	5.6 ± 0.5
Alkhajah et al. (2012)	4.5 ± 0.9	1.5 ± 0.4	2.7 ± 0.7	0.9 ± 0.8	4.9 ± 0.4		
Ashe et al. (2015)							
Balducci et al. (2019)	4.7 ± 1.0	1.2 ± 0.4	2.9 ± 0.9	1.5 ± 0.9 [a]	7.6 ± 2.7	77.4 ± 74.7 [a]	7.4 ± 1.5
Biddle et al. (2015)	4.9 ± 1.0	1.3 ± 0.3	3.0 ± 0.7	1.5 ± 1.2	4.8 ± 0.6	86 ± 56.5	5.6 ± 0.3
Butler (2018)							5.4 ± 2.5
Carr et al. (2013)	4.9 ± 0.7	1.2 ± 0.5	3.0 ± 0.7	1.3 ± 0.6			
Danquah et al. (2017)							
Dunning (2018)	4.8 ± 0.8	1.6 ± 0.3	2.8 ± 0.7	1.0 ± 0.5	4.7 ± 0.4	37.1 ± 15.2	
Garland (2018)							
Graves et al. (2015)	4.2 ± 0.9			1.6 ± 0.7	5.1 ± 0.7		
Healy et al. (2013)	5 ± 0.9	1.5 ± 0.4	2.9 ± 0.8	1.1 ± 0.5	4.8 ± 0.9	52.7 ± 28.9	
Healy et al. (2017)	5.4 ± 1.0	1.5 ± 0.4	3.2 ± 0.9	1.4 ± 0.7	5.1 ± 1.4	61.4 ± 112	
Kallings et al. (2009)	5.5 ± 0.1	1.7 ± 0.1	3.3 ± 0.1	1.3 ± 0.1	5.4 ± 0.1		4.9 ± 0.1
Kozey-Keadle et al. (2014)	4.7 ± 0.8	1.7 ± 0.5		1.9 ± 1.2	5.8 ± 0.7	133 ± 86.6	
Lin et al. (2017)	5 ± 0.9	1.5 ± 0.4	2.8 ± 0.7	1.3 ± 0.7	4.8 ± 0.7	42.6 ± 31.2	
Lyons et al. (2017)							
MacEwen et al. (2017)	5.1 ± 0.9	1.5 ± 0.4	2.9 ± 0.7	1.6 ± 0.8	5.8 ± 0.5		6.9 ± 0.5
Mainsbridge et al. (2014)							
Malaeb et al. (2019)							
Mantzari et al. (2018)	4.8 ± 1.0	1.4 ± 0.3	2.7 ± 1.0	1.4 ± 0.6			5.2 ± 2.4
Maxwell-Smith et al. (2018)							
Maylor et al. (2018)	4.4 ± 0.4	1.4 ± 0.2					
Miyamoto et al. (2017)	5.3 ± 0.2		3.3 ± 0.2	1.2 ± 0.1	7.0 ± 0.4		7.0 ± 0.2
Pesola et al. (2017)	4.8 ± 0.8	1.8 ± 0.5	2.6 ± 0.9	1.0 ± 0.9	5.3 ± 0.5	38.2 ± 25.6	
Peterman et al. (2019)	4 ± 0.8	1.1 ± 0.2	2.5 ± 0.7	1.2 ± 0.6	4.1 ± 0.6		

Puig-Ribera et al. (2015)							
Resendiz et al. (2019)							
Schuna et al. (2014)							
Taylor et al. (2016) - Booster breaks	5.0 ± 0.4	1.4 ± 0.2	2.9 ± 0.3	1.4 ± 0.5	5.4 ± 2.1		
Taylor et al. (2016) - Computer breaks	4.8 ± 0.3	1.3 ± 0.2	2.8 ± 0.3	1.3 ± 0.3	5.3 ± 1.3		
Thomsen et al. (2016)	5.5 ± 1.3	1.5 ± 0.4	3.1 ± 1.1	1.4 ± 0.7			5.2 ± 0.1
Thomsen et al. (2017)	5.2 ± 1.1	1.6 ± 0.5	3.1 ± 0.9	1.2 ± 0.6			5.5 ± 0.8
Zhu et al. (2018)	4.7 ± 0.7	1.6 ± 0.5	2.9 ± 0.7	1.1 ± 0.6	5.4 ± 0.7	73.6 ± 41.4	

TC = Total Cholesterol; HDL = High-density lipoprotein cholesterol; LDL = Low-density lipoprotein cholesterol; TG = triglycerides

[a] Different value reported in relation to the interim outcomes in Balducci 2017: 1.8 ± 1.4 mM triglycerides and 89.5 ± 86.4 pM insulin.

Supplementary Table S6 Individual study risk of bias assessment for 1) anthropometric and blood pressure, 2) glucose, and; 3) lipid measures.

No.	Study	Bias arising from the randomisation process			Bias due to deviations from intended intervention			Bias due to missing outcome data			Bias in measurement of the outcome			Bias in selection of the reported result			Overall bias		
	Measure	*1*	*2*	*3*	*1*	*2*	*3*	*1*	*2*	*3*	*1*	*2*	*3*	*1*	*2*	*3*	*1*	*2*	*3*
1	Aadahl 2014	+	+	+	+	+	+	?	?	?	+	+	+	+	+	+	?	?	?
2	Alkhajah 2012	-	-	-	+	+	+	?	-	-	+	+	+	+	+	+	-	-	-
3	Ashe 2015	?			?			?			+			+			?		
4	Balducci, 2019*	+	+	+	+	+	+	+	+	+	+	+	+	-	-	+	-	-	+
5	Biddle 2015	+	+	+	+	+	+	?	?	?	+	+	+	+	+	+	?	?	?
6	Butler 2018	?	?	?	-	-	-	+	+	+	?	+	+	+	+	?	-	-	-
7	Carr 2013	+		+	+		+	?		?	+		+	?		+	?		?
8	Danquah 2017	+			+			+			+			+			+		
9	Dunning, 2018	+	+	+	?	?	?	+	+	+	?	?	?	+	+	+	?	?	?
10	Garland, 2018	-			+			-			-			+			-		
11	Graves 2015	+	+	+	+	+	+	+	+	+	+	+	+	?	?	?	?	?	?
12	Healy 2013	-	-	-	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-
13	Healy 2017	+	+	+	+	+	+	?	?	?	+	+	+	+	+	+	?	?	?
14	Kallings 2009	?	?	?	+	+	+	+	+	+	+	+	+	+	+	+	?	?	?
15	Kozey Keadle 2014	-	-	-	-	-	-	?	?	?	+	+	+	+	+	+	-	-	-
16	Lin 2017	?	?	?	+	+	+	?	?	?	+	+	+	+	+	+	?	?	?
17	Lyons 2017	+			+			+			+			+			+		
18	MacEwen 2017	+	+	+	-	-	-	?	?	?	+	+	+	+	+	+	-	-	-
19	Mainsbridge 2014	?			+			+			?			?			?		
20	Malaeb, 2019	-			-			-			?			-			-		
21	Mantzari, 2018	?	?	?	?	?	?	+	+	+	+	+	+	+	+	+	?	?	?
22	Maxwell-Smith 2019	?			+			+			+			+			?		
23	Maylor, 2018	+		+	?		?	+		+	?		?	+		+	?		?
24	Miyamoto 2017	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
25	Pesola 2017	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
26	Peterman, 2019	?	?	?	+	+	+	-	-	-	?	+	+	-	-	-	-	-	-
27	Puig-Ribera 2015	?			+			?			+			+			?		
28	Resendiz, 2019	?			?			+			?			+			?		
29	Schuna 2014	?			+			+			+			+			?		
30	Taylor 2016	?	?	?	?	?	?	?	?	?	?	?	?	+	+	+	?	?	?
31	Thomsen 2016	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
32	Thomsen 2017	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
33	Zhu, 2018	-	-	-	+	+	+	-	-	-	?	+	+	+	+	+	-	-	-
Total	Low Risk (+)	15	11	13	23	15	16	18	11	12	23	19	20	27	18	20	6	4	5
Total	Unclear risk (?)	12	6	6	6	3	4	11	7	8	9	2	3	3	1	2	17	9	11
Total	High risk (-)	6	4	4	4	3	3	4	3	3	1	0	0	3	2	1	10	8	7
Total	All	33	21	23	33	21	23	33	21	23	33	21	23	33	21	23	33	21	23

Notes: 1=anthropometry & blood pressure outcomes; 2=glucose metabolism outcomes; 3=lipid metabolism outcomes; + = low risk of bias; ? = unclear risk of bias (some concerns); – = high risk of bias.

* Data were extracted from the earlier paper related to this study (Balducci 2017) when it was not reported in the 2019 paper (%BF; FFM; BMI; fasting insulin; HOMA). Risk of bias for Balducci 2017 was low for all criteria.

Supplemental Table S7 Assumption tests regarding publication bias

Outcome	Begg's test
Weight, kg	z = -0.21, p = 0.870
Body Mass Index, kg/m^2	z = -0.57, p = 0.602
Waist circumference, cm	z = 1.40, p = 0.162
Body fat, % of body weight	z = 0.68, p = 0.499
Fat mass, kg	z = 1.13, p = 0.260
Fat-free mass, kg	z = -1.20, p = 0.368
Systolic BP, mmHg	z = -0.49, p = 0.657
Diastolic BP, mmHg	z = -1.38, p = 0.183
Glucose, mM	z = 0.70, p = 0.484
Insulin, pM	z = 0.36, p = 0.721
HbA1c, %	z = -0.52, p = 0.754
Total cholesterol, mM	z = -0.71, p = 0.509
HDL cholesterol, mM	z = 0.08, p = 0.932
LDL cholesterol, mM	z = -0.68, p = 0.538
Triglycerides, mM	z = 1.35, p = 0.177

Table S8: Meta-regression: associations of study characteristics with intervention effects on cardiometabolic biomarkers displaying low heterogeneity

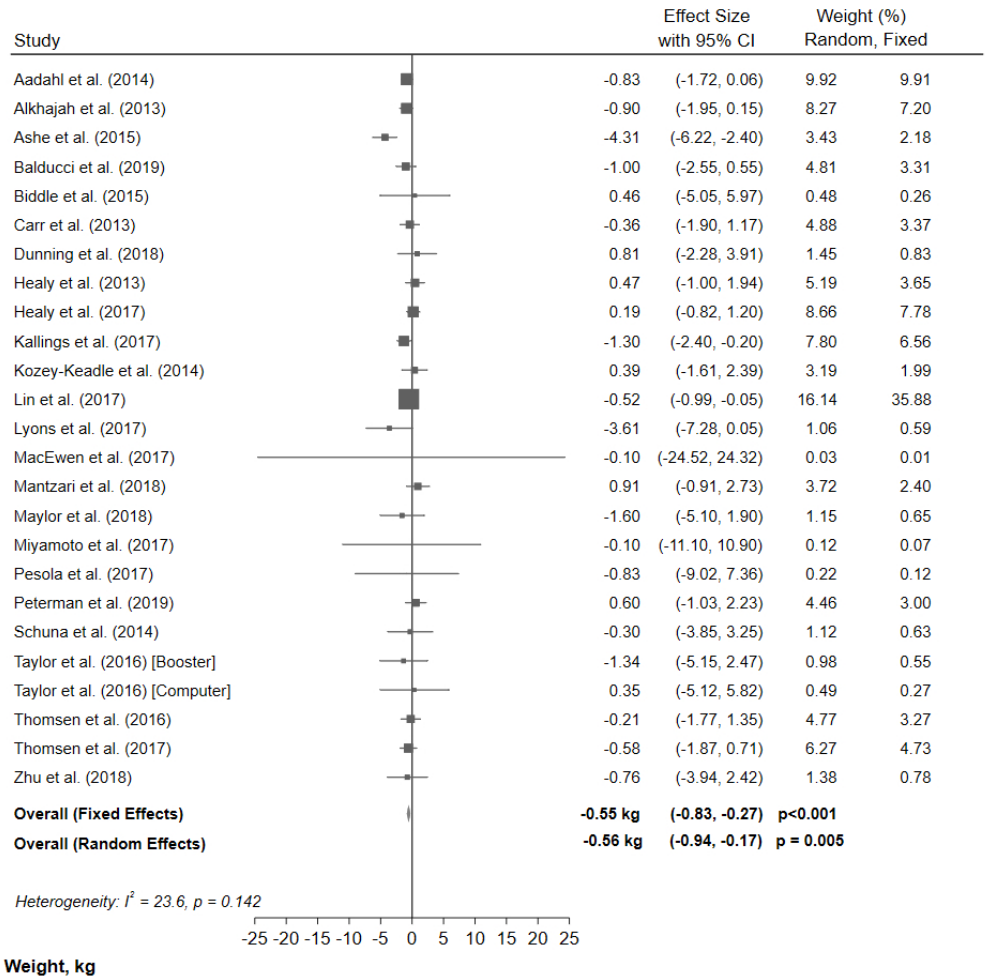
	Unadjusted				Age adjusted			
	k, N	**b (95% CI)**	**p**	**I^2, p**	**n, N**	**b (95% CI)**	**p**	**I^2, p**
Weight (kg)	**25, 1839**			**23.6%, p=0.142**	**25, 1839**			**23.6%, p=0.142**
Mean baseline age, per 10 y	25, 1839	-0.51 (-0.84, -0.18)	0.002	0.0%, p = 0.504		-	-	-
Mean baseline BMI, kg/m^2	25, 1839	-0.02 (-0.15, 0.10)	0.731	26.6%, p = 0.115	25, 1839	0.03 (-0.07, 0.12)	0.579	0.0%, p = 0.462
Mean baseline level	25, 1839	0.00 (-0.04, 0.05)	0.873	26.8%, p = 0.113	25, 1839	0.02 (-0.01, 0.05)	0.313	0.0%, p = 0.505
Sedentary effectiveness, h/day	25, 1839	-0.17 (-0.84, 0.50)	0.625	26.6%, p = 0.115	25, 1839	-0.14 (-0.61, 0.33)	0.565	0.0%, p = 0.463
Duration (vs ≤3 months)	25, 1839		*0.036*	28.0%, p = 0.106	25, 1839		*0.009*	2.4%, p = 0.428
3–6 months		-1.26 (-2.25, -0.27)	0.012			-0.60 (-1.47, 0.26)	0.173	
>6 months		-0.00 (-1.15, 1.15)	0.997			0.25 (-0.66, 1.15)	0.591	
Risk of bias (vs High risk)	25, 1839		*0.640*	29.1%, p = 0.096	25, 1839		*0.020*	5.6%, p = 0.385
Some concerns		-0.47 (-1.85, 0.91)	0.507			0.67 (-0.69, 2.03)	0.335	
Low risk		-0.43 (-1.37, 0.51)	0.366			0.17 (-0.66, 1.00)	0.692	
Body fat percentage, %	**16, 1618**			**5.5%, p=0.390**	**16, 1618**			**5.5%, p=0.390**
Mean baseline age, per 10 y	16, 1618	-0.13 (-0.38, 0.13)	0.325	6.5%, p = 0.380		-	-	-
Mean baseline BMI, kg/m^2	16, 1618	-0.04 (-0.13, 0.05)	0.397	8.5%, p = 0.358	16, 1618	-0.02 (-0.14, 0.10)	0.732	13.0%, p = 0.311
Mean baseline level	16, 1618	-0.04 (-0.10, 0.01)	0.130	0.0%, p = 0.482	16, 1618	-0.04 (-0.11, 0.03)	0.238	3.9%, p = 0.408
Sedentary effectiveness, h/day	16, 1618	-0.21 (-0.75, 0.34)	0.456	8.9%, p = 0.354	16, 1618	-0.31 (-0.88, 0.25)	0.274	5.8%, p = 0.388
Duration (vs ≤3 months)	16, 1618		*0.194*	16.2%, p = 0.276	16, 1618		*0.257*	12.1%, p = 0.323
3–6 months		-0.56 (-1.19, 0.06)	0.078			-0.48 (-1.11, 0.16)	0.143	
>6 months		-0.06 (-0.77, 0.66)	0.880			0.11 (-0.67, 0.89)	0.786	
Risk of bias (vs High risk)	16, 1618		*0.209*	16.3%, p = 0.276	16, 1618		*0.332*	17.5%, p = 0.267
Some concerns		-0.76 (-1.61, 0.09)	0.081			-0.68 (-1.57, 0.21)	0.132	
Low risk		-0.51 (-1.38, 0.35)	0.243			-0.44 (-1.34, 0.45)	0.331	
Fat mass, kg	**6, 724**			**26.6%, p=0.235**	**6, 724**			**26.6%, p=0.235**
Mean baseline age, per 10 y	6, 724	-0.22 (-0.64, 0.19)	0.296	26.7%, p = 0.243		-	-	-
Mean baseline BMI, kg/m^2	6, 724	-0.12 (-0.30, 0.06)	0.179	17.1%, p = 0.306	6, 724	-0.10 (-0.34, 0.14)	0.416	35.4%, p = 0.200

Mean baseline level	6, 724	-0.08 (-0.18, 0.01)	0.082	0.0%, p = 0.436	6, 724	-0.09 (-0.22, 0.05)	0.212	20.6%, p = 0.286
Sedentary effectiveness, h/day	6, 724	-0.67 (-1.71, 0.36)	0.202	22.8%, p = 0.269	6, 724	-0.78 (-1.72, 0.16)	0.104	0.0%, p = 0.422
Duration (vs ≤3 months)	6, 724		*0.506*	55.6%, p = 0.080	6, 724		*0.685*	63.1%, p = 0.067
3–6 months		-0.83 (-2.24, 0.58)	0.247			-1.61 (-5.37, 2.16)	0.403	
>6 months		-0.06 (-1.45, 1.33)	0.930			-0.20 (-1.74, 1.35)	0.804	
Risk of bias (vs High risk)	6, 724		*0.637*	50.3%, p = 0.110	6, 724		*0.837*	63.1%, p = 0.066
Some concerns		-0.30 (-1.48, 0.89)	0.624			-0.22 (-1.75, 1.31)	0.778	
Low risk		-0.56 (-1.73, 0.60)	0.344			-0.37 (-2.37, 1.63)	0.716	
Systolic Blood Pressure, mmHg	**25, 1932**			**8.6%, p=0.341**	**25, 1932**			**8.6%, p=0.341**
Mean baseline age, per 10 y	25, 1932	0.38 (-0.49, 1.24)	0.392	8.1%, p = 0.349		-	-	-
Mean baseline BMI, kg/m^2	24, 1903	0.02 (-0.29, 0.34)	0.882	15.1%, p = 0.256	24, 1903	-0.02 (-0.35, 0.32)	0.922	15.7%, p = 0.251
Mean baseline level	24, 1911	0.04 (-0.11, 0.18)	0.617	4.3%, p = 0.402	24, 1911	0.12 (-0.11, 0.36)	0.303	4.8%, p = 0.396
Sedentary effectiveness, h/day	23, 1882	-0.48 (-2.16, 1.20)	0.573	7.9%, p = 0.355	23, 1882	-0.71 (-2.64, 1.22)	0.472	11.3%, p = 0.312
Duration (vs ≤3 months)	25, 1932		*0.708*	14.7%, p = 0.261	25, 1932		*0.743*	14.0%, p = 0.273
3–6 months		0.31 (-2.49, 3.10)	0.828			0.16 (-2.67, 2.99)	0.912	
>6 months		-1.09 (-4.01, 1.84)	0.466			-1.19 (-4.13, 1.76)	0.430	
Risk of bias (vs High risk)	25, 1932		*0.375*	10.8%, p = 0.313	25, 1932		*0.607*	12.9%, p = 0.288
Some concerns		1.54 (-1.57, 4.65)	0.332			1.40 (-2.10, 4.90)	0.433	
Low risk		1.80 (-0.76, 4.36)	0.168			1.66 (-1.21, 4.53)	0.258	
HDL Cholesterol, mM	**22, 1760**			**22.5%, p=0.168**	**22, 1760**			**22.5%, p=0.168**
Mean baseline age, per 10 y	22, 1760	-0.01 (-0.03, 0.00)	0.011	0.7%, p = 0.450		-	-	-
Mean baseline BMI, kg/m^2	22, 1760	0.00 (-0.01, 0.00)	0.304	14.3%, p = 0.273	22, 1760	-0.00 (-0.01, 0.01)	0.768	5.2%, p = 0.392
Mean baseline level	21, 1739	-0.08 (-0.23, 0.08)	0.344	6.3%, p = 0.378	21, 1739	-0.06 (-0.22, 0.09)	0.428	7.4%, p = 0.365
Sedentary effectiveness, h/day	21, 1739	-0.02 (-0.06, 0.01)	0.222	3.3%, p = 0.416	21, 1739	-0.04 (-0.08, 0.00)	0.046	0.0%, p = 0.583
Duration (vs ≤3 months)	22, 1760		*0.266*	27.6%, p = 0.124	22, 1760		*0.163*	10.6%, p = 0.325
3–6 months		-0.05 (-0.12, 0.01)	0.104			-0.04 (-0.10, 0.02)	0.175	
>6 months		-0.02 (-0.08, 0.05)	0.604			-0.01 (-0.07, 0.05)	0.735	
Risk of bias (vs High risk)	22, 1760		*0.023*	9.6%, p = 0.335	22, 1760		*0.035*	5.2%, p = 0.392

Some concerns		-0.06 (-0.12, 0.00)	0.035			-0.09 (-0.18, 0.01)	0.076	
Low risk		-0.06 (-0.10, -0.01)	0.015			-0.07 (-0.14, 0.00)	0.043	

Table presents unstandardized regression coefficient (*b*) and 95% confidence interval (CI) and *p* value from meta-regression of controlled trials of adult sedentary behaviour interventions ≥7 days. Italics indicates overall p value (omnibus test). No meta-regression performed for BMI or LDL cholesterol, since $I^2=0$.

[a] k = total number of interventions included and n = total number of individuals analysed in the included interventions, in the meta-regressions or main metaanalysis (boldface) [b] Residual heterogeneity (I^2 and p from Cochrane's Q test) with overall heterogeneity in the main metaanalysis shown in boldface



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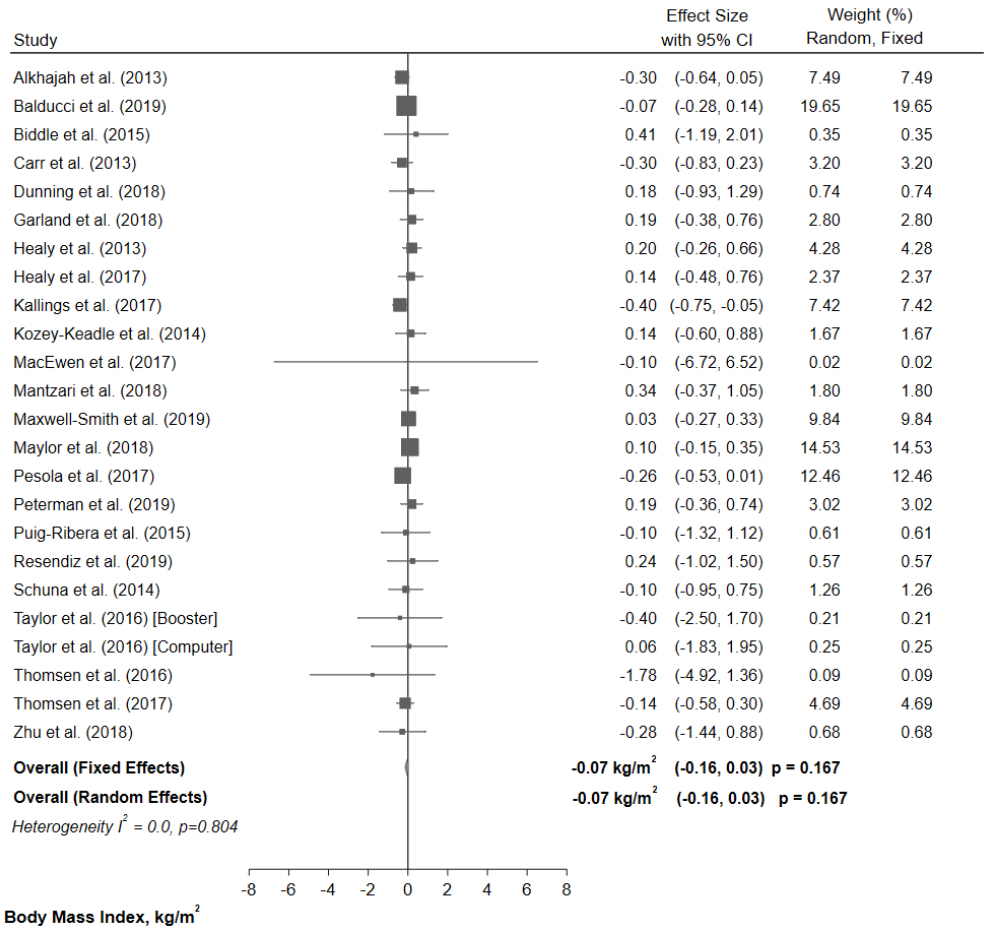

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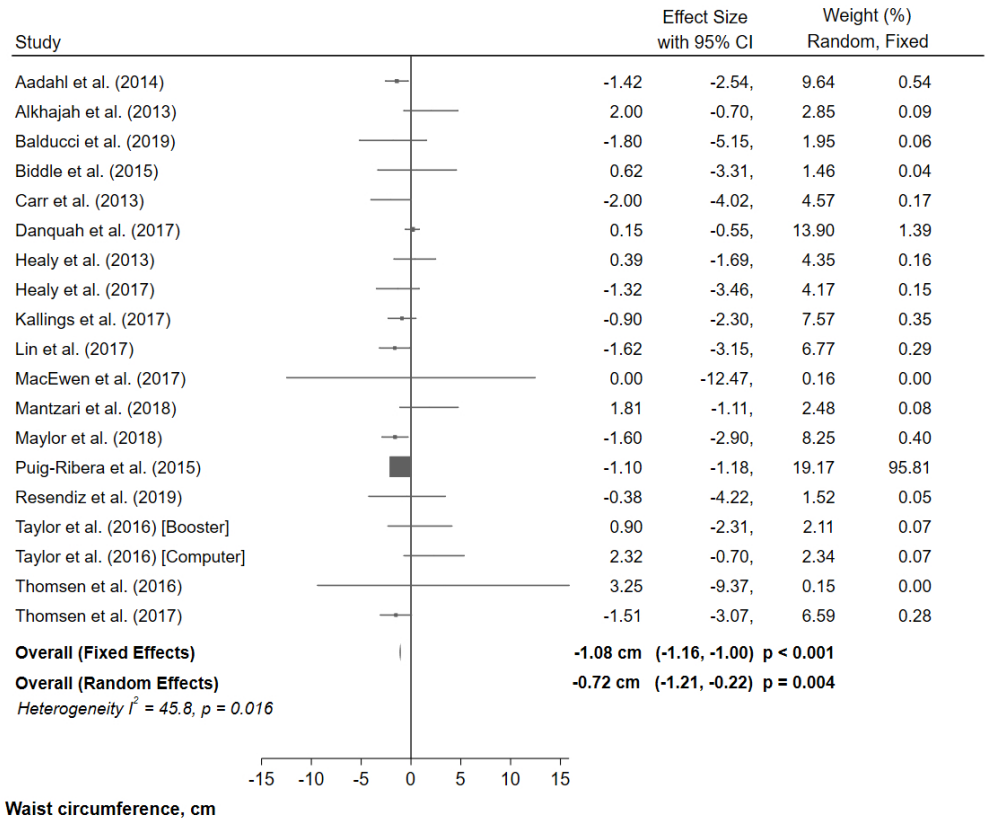

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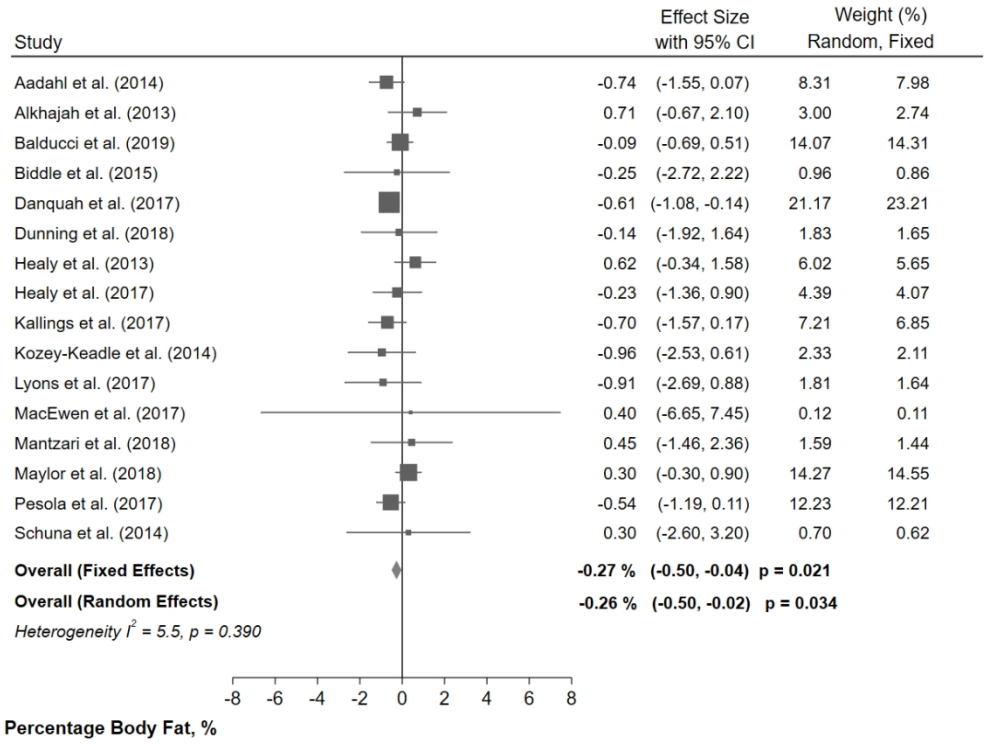

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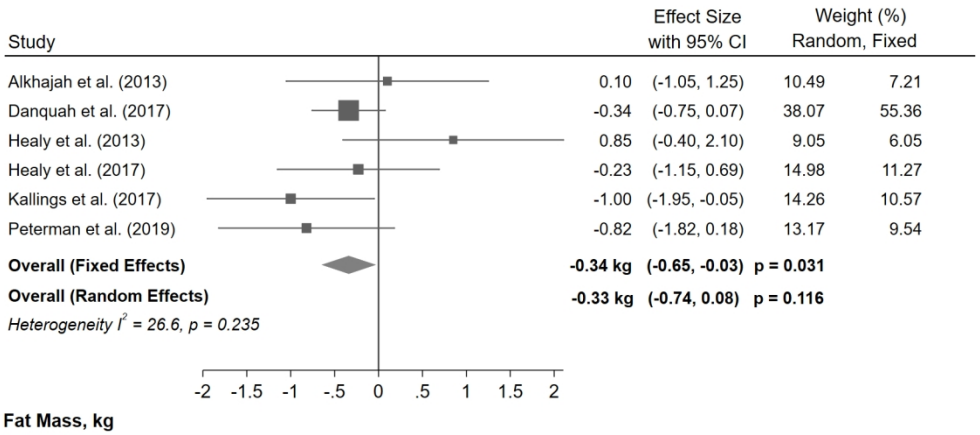

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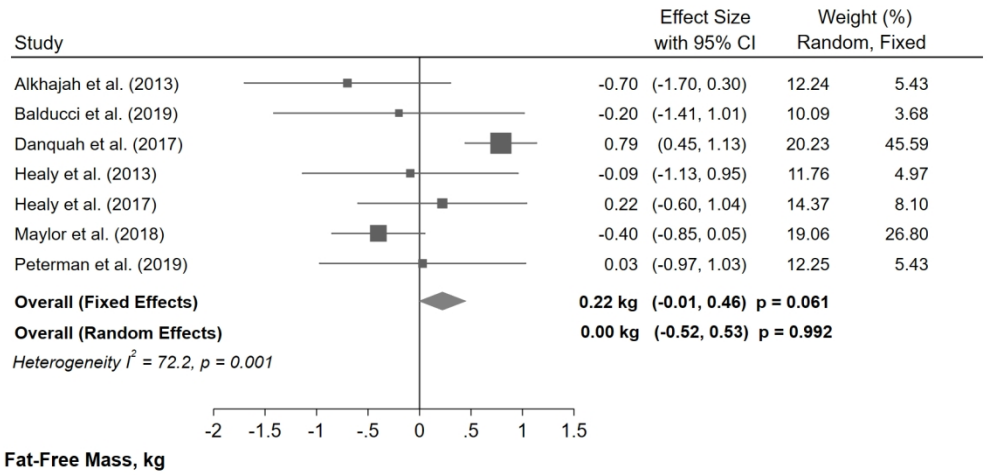

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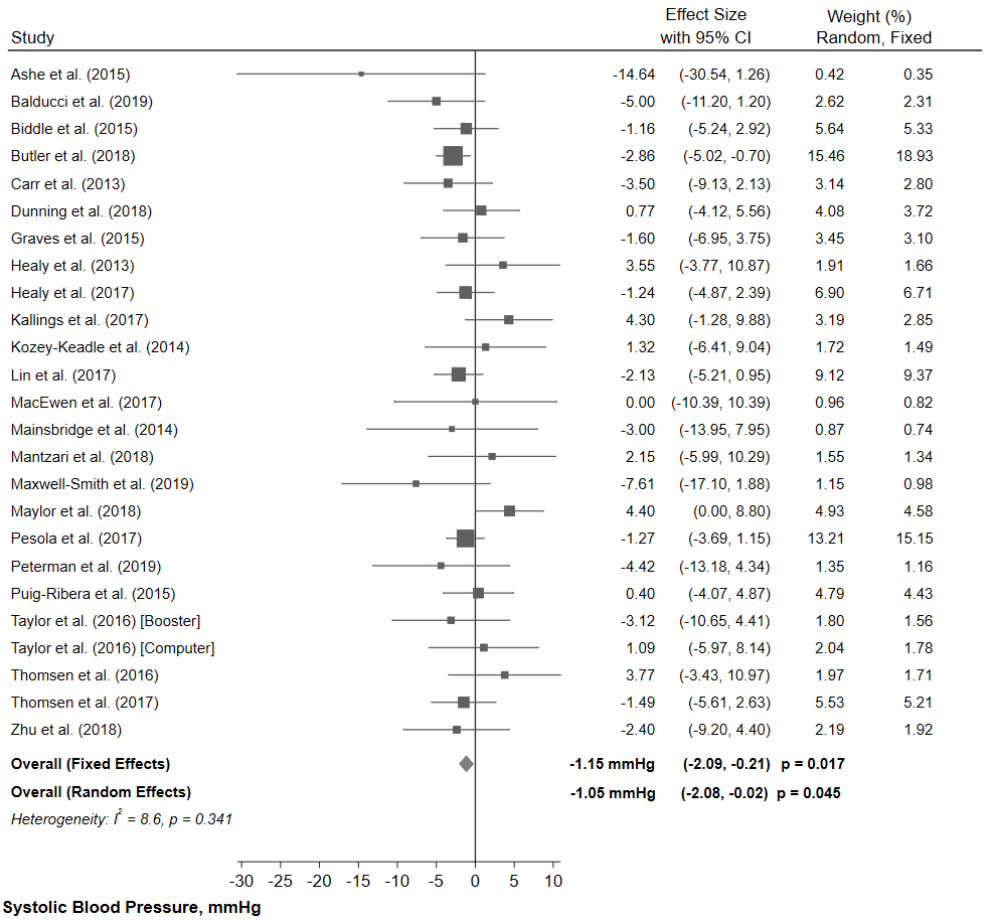

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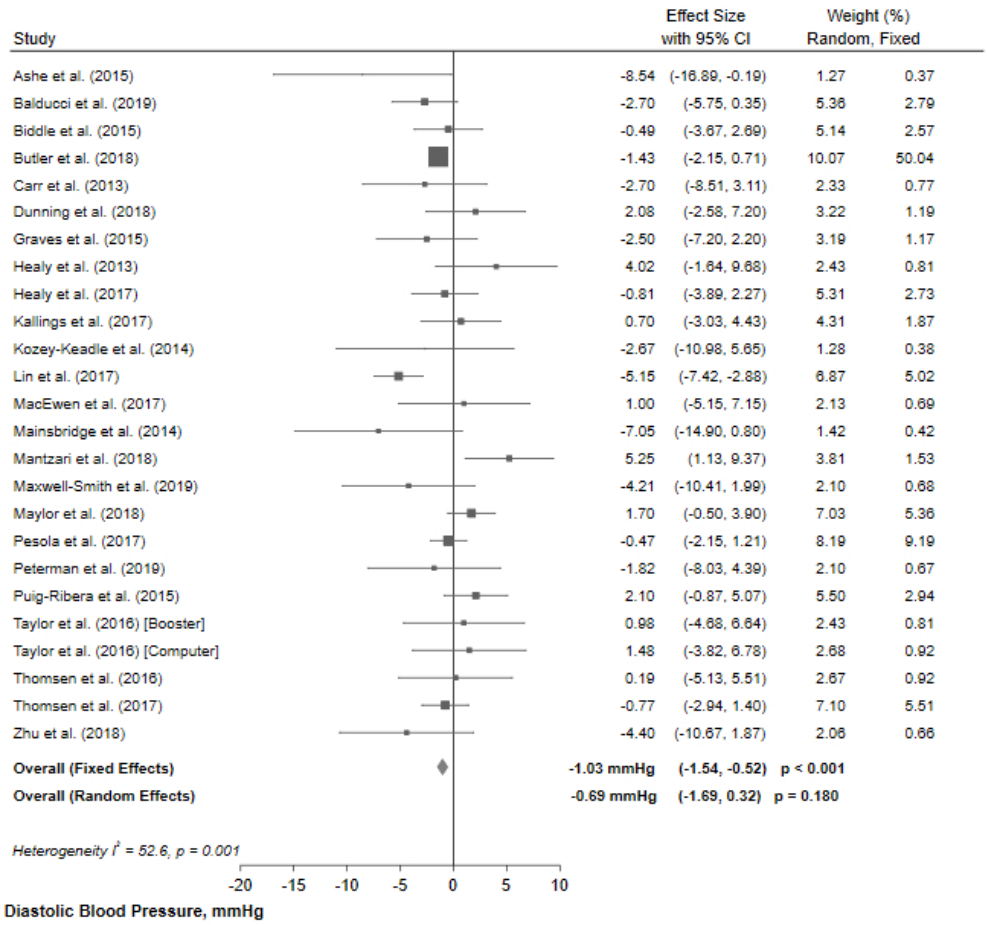

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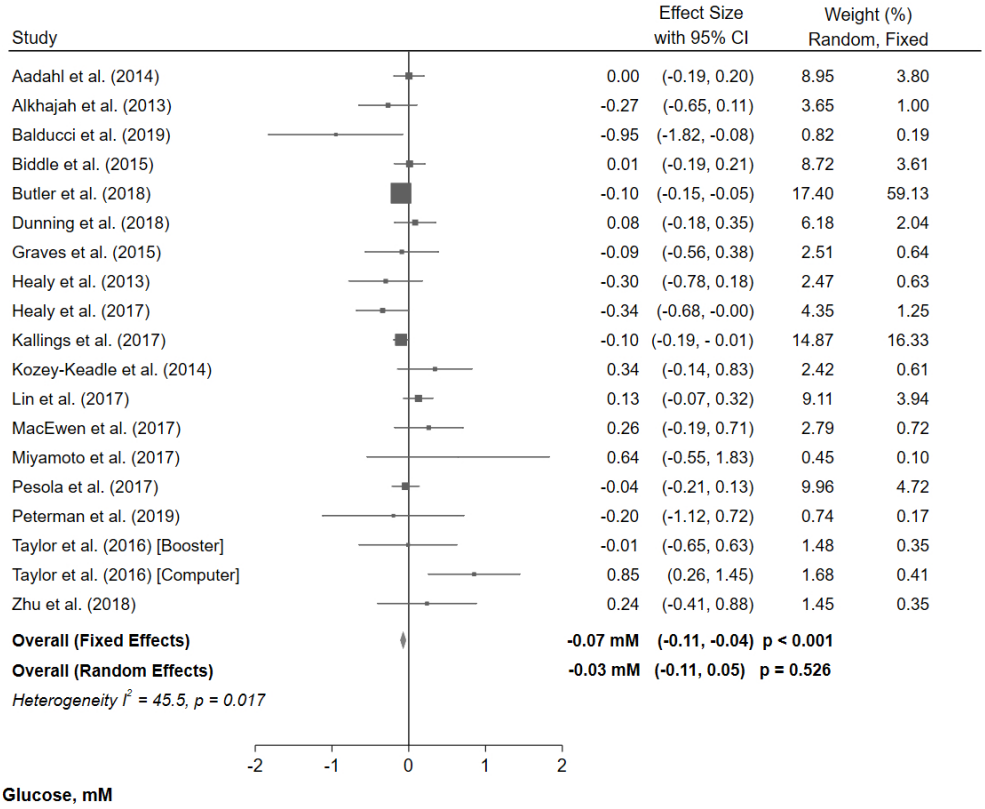

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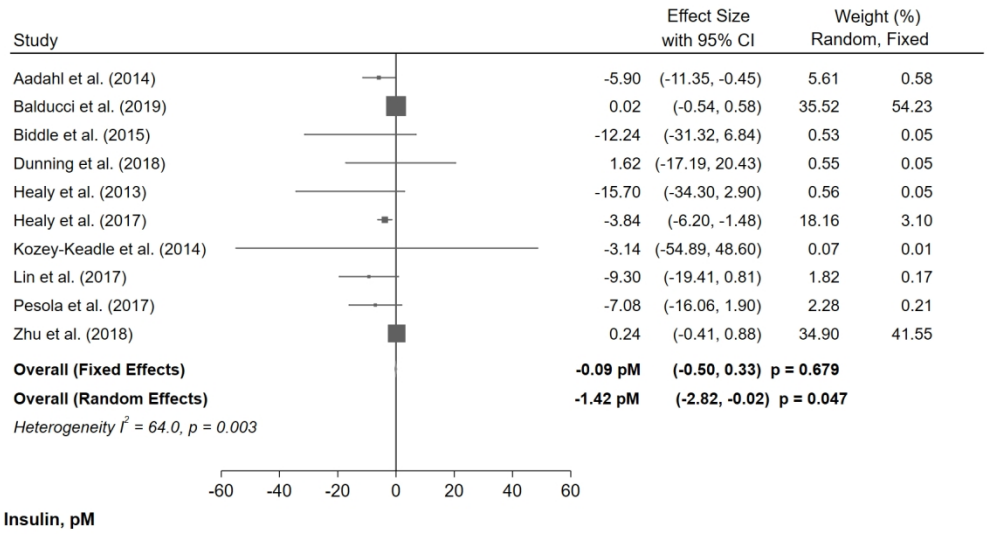

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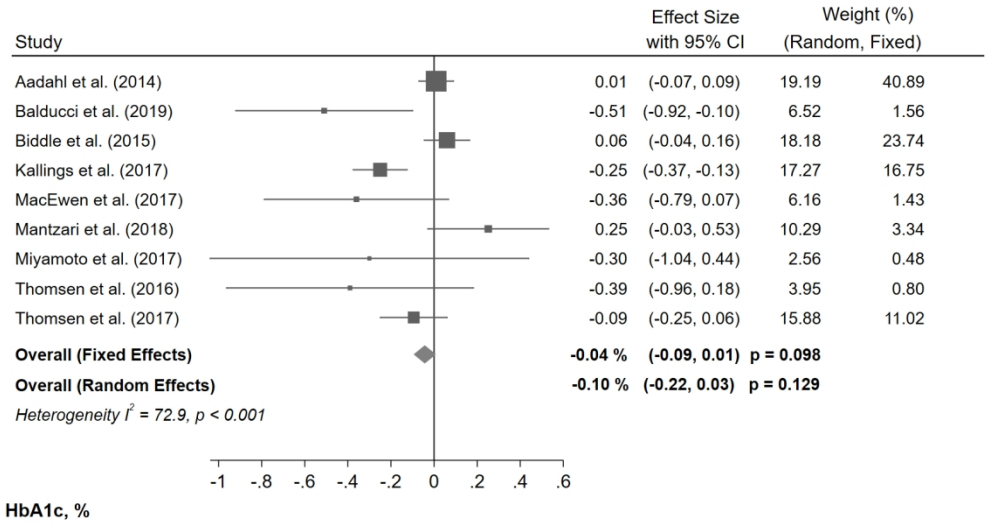

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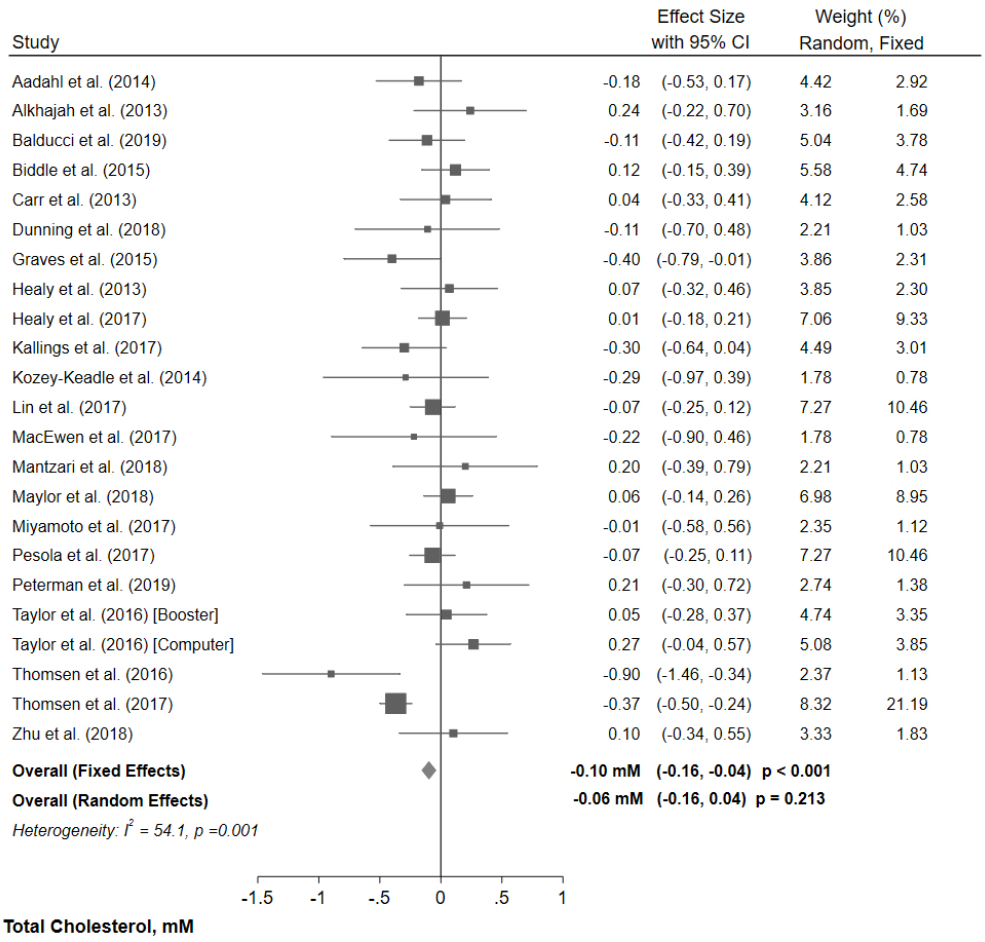
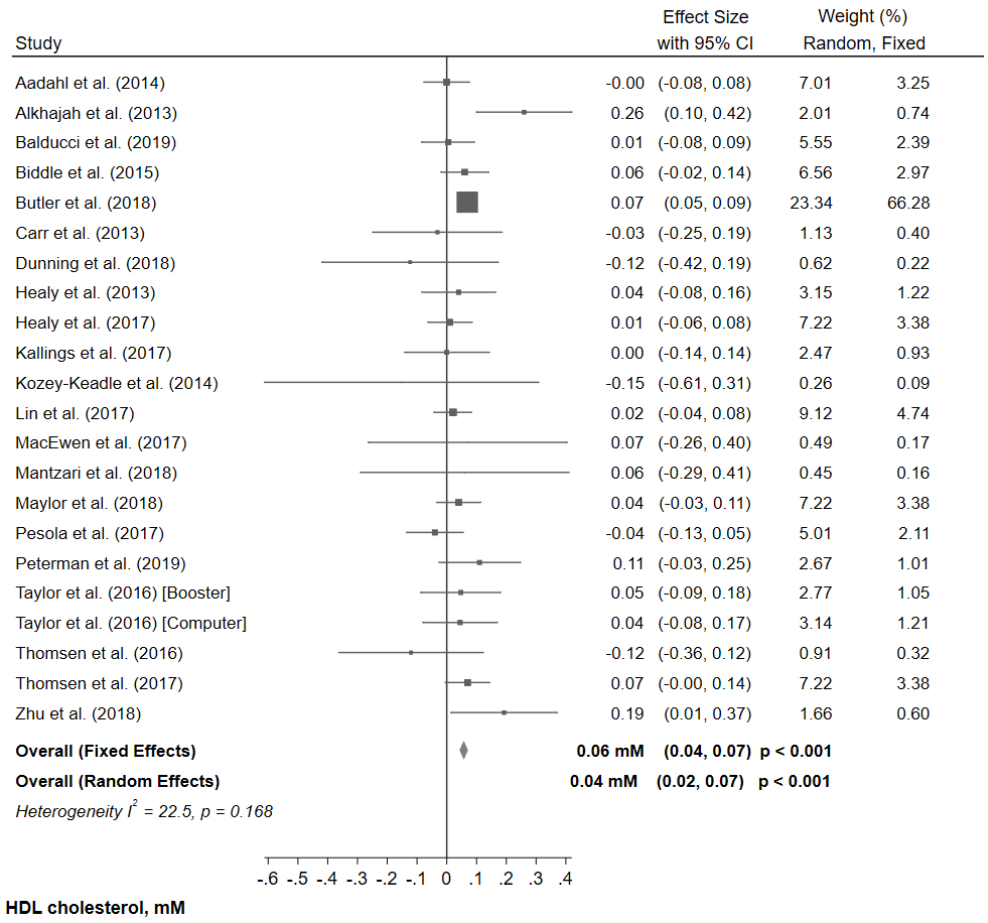
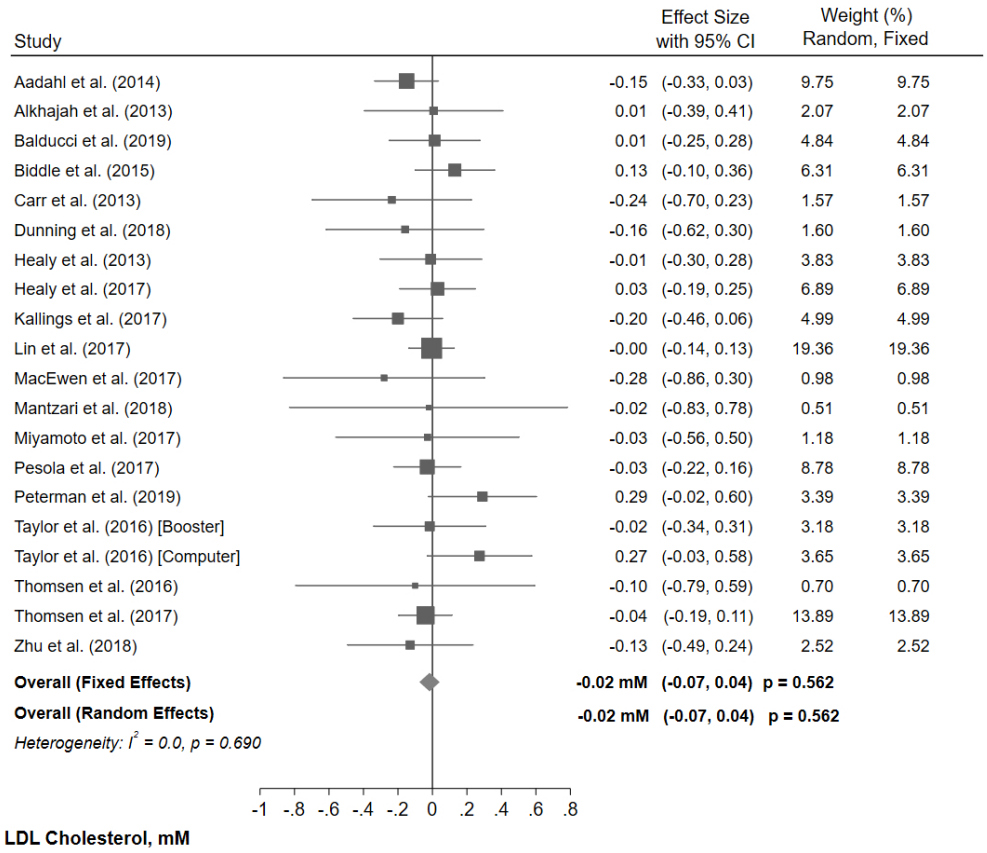


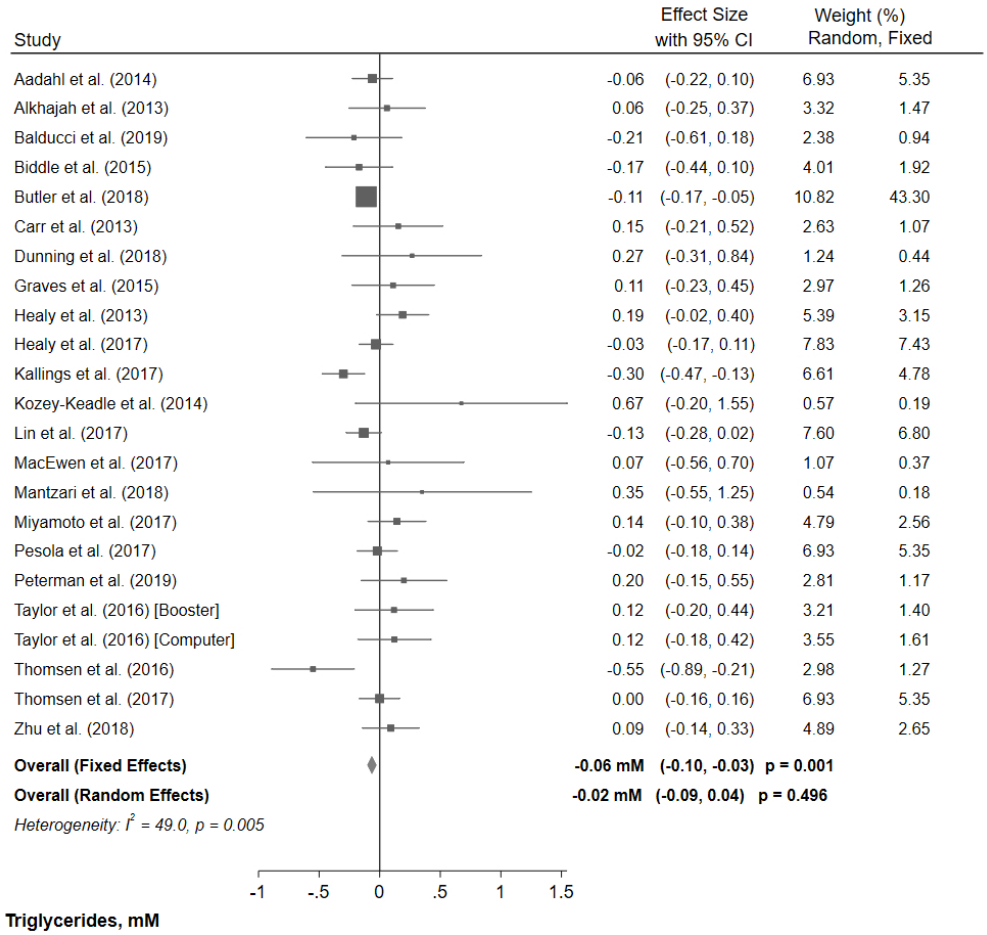
343x326mm (72 x 72 DPI)



350x326mm (72 x 72 DPI)



379x326mm (72 x 72 DPI)



345x326mm (72 x 72 DPI)